

HÖGER OCH VÄNSTER KAMMARES EJEKTIONSFRAKTION I VILA OCH UNDER ARBETE BESTÄMD MED RADIONUKLID-ANGIOKARDIOGRAFI

Metodologiska synpunkter samt jämförelse med samtidigt
erhållna kateteriseringsresultat vid pulmonell hypertension
och vid ischemisk hjärtsjukdom

Jan Anders Dahlström

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RIGHT AND LEFT VENTRICULAR EJECTION FRACTION AT REST AND DURING EXERCISE ASSESSED WITH RADIONUCLIDE ANGIOCARDIOGRAPHY. Methodological aspects and comparison to simultaneously obtained catheterization results in pulmonary hypertension and in ischemic heart disease.

Right (RVEF) and left ventricular ejection fraction (LVEF) assessed with radionuclide angiocardiology were compared to simultaneously obtained catheterization results at rest and during exercise in patients with pulmonary hypertension and ischemic heart disease. Methodological aspects of EF measurements were also investigated.

Blood pool imaging was performed with red blood cells (RBC) labelled with $^{99}\text{Tc}^{\text{m}}$ in vivo as this method gave more stable $^{99}\text{Tc}^{\text{m}}$ levels in blood compared to $^{99}\text{Tc}^{\text{m}}$ -labelled human serum albumin and because it was more convenient than labelling RBC in vitro. RVEF measured with first pass (FP) technique and equilibrium (EQ) technique correlated well at rest, $r = 0.86$, and during exercise, $r = 0.91$. The FP technique had the best reproducibility and reference values at rest were $49 \pm 5\%$ increasing with exercise. When $^{99}\text{Tc}^{\text{m}}$ and ^{133}Xe were compared to assess RVEF with FP technique, the correlation was good, $r = 0.88$. LVEF assessed with EQ technique and a fixed end-diastolic region of interest was very reproducible at rest and during exercise; reference values at rest were $56 \pm 8\%$ increasing with exercise.

In 10 patients with pulmonary hypertension significant negative correlations were found between RVEF assessed with FP technique and pressures in pulmonary artery and right atrium. Abnormal RVEF was found in all patients with right ventricular dysfunction. In 22 patients with recent myocardial infarction measurements of LVEF detected left ventricular dysfunction better than did measurement of pulmonary artery diastolic pressure. During effort angina in another 10 patients all had abnormal LVEF and abnormal hemodynamics. By combining ejection fraction and stroke volume, ventricular volumes were calculated at rest and during exercise.

Key words

Angina pectoris; exercise test; heart catheterization; heart function test; hypertension, pulmonary; myocardial infarction; radionuclide imaging; xenon radioisotopes.

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Denna studie har erhållit ekonomiskt stöd från Malmö Sjukvårdsförvaltnings fonder, från Medicinska Fakulteten vid Lunds Universitet, Svenska Nationalföreningen mot Hjärt- och Lungsjukdomar samt från Riksföreningen mot Cancer.



Denna avhandling utgör en sammanfattning av följande uppsatser:

- I. Cardiac Blood Pool Imaging - A Clinical Comparison between Red Blood Cells Labeled with ^{99m}Tc in vivo and in vitro and ^{99m}Tc -labeled Human Serum Albumin.
Nuclear Medicine 18: 271-273, 1979.
Tillsammans med S. Carlsson, B. Lilja, S. Mattsson och C. Pettersson.
- II. Radionuclide Assessment of Right Ventricular Ejection Fraction - A Comparison of First Pass Studies with ^{133}Xe and ^{99m}Tc .
Accepterad för publicering i Clinical Physiology.
- III. Simultaneous Assessment of Right Ventricular Ejection Fraction and Central Hemodynamics at Rest and during Exercise in Patients with Pulmonary Hypertension.
Insänd till Clinical Physiology.
- IV. Left Ventricular Function after Myocardial Infarction.
Accepterad för publicering i International Journal of Cardiology.
Tillsammans med O. Ohlsson och B. Lilja.
- V. Left Ventricular Function at Rest and during Exercise in Coronary Insufficiency - A Simultaneous Evaluation by means of Radionuclide Angiocardiology and Catheterization.
Accepterad för publicering i Clinical Physiology.
Tillsammans med B. Lilja, O. Ohlsson och A. Torp.

I den följande presentationen sker hänvisning till dessa uppsatser med deras romerska siffror.

Genomförandet av denna undersökning har varit helt beroende av tillmötesgående och förstående patienter samt av goda råd, vänlig hjälp, stöd och uppmuntran, aktivt deltagande och konstruktiv kritik från vänner och arbetskamrater, vilka jag hjärtligen tackar.

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FÖRKORTNINGAR

LVEF	= vänster kammares ejektionsfraktion
LVEDVI	= vänster kammares slutdiastoliska volymindex
LVESVI	= vänster kammares slutsystoliska volymindex
LVFP	= vänster kammares fyllnadstryck
RVEF	= höger kammares ejektionsfraktion
SI	= slagvolymindex
SWI	= vänster kammares slagarbetsindex

INLEDNING

Av tradition har hjärtfunktionen värderats med mätning av kammartryck och blodflöden (Jonsson 1967). Speciellt kammarens slutdiastoliska tryck, s.k. fyllnadstryck, slagvolym och slagarbete har använts för att beskriva hjärtfunktionen (Sonnenblick & Strobeck 1977). Dessa mätningar fordrar hjärkateterisering. Sådant behövs även då röntgenologisk teknik, s.k. angiokardiografi, används för värdering av kammarfunktionen med mätning av kammarvolym och ejektionsfraktioner, d.v.s.:

$$\frac{(\text{slutdiastolisk volym} - \text{slutsystolisk volym})}{\text{slutdiastolisk volym.}}$$

Speciellt vänster kammars ejektionsfraktion (LVEF) har rönt stort intresse och visat sig ha stort kliniskt värde för bl.a. bedömning av prognosen vid hjärtsjukdomar (Cohn et al. 1974; Nelson et al. 1975). Den röntgenologiska tekniken för volymsmätning antar att vänster kammare är en ellipsoid, varefter volymen uträknas enligt en area-längd-metod (Sandler & Dodge 1968). Även höger kammars ejektionsfraktion (RVEF) kan beräknas med röntgenologisk teknik men då antages andra mer komplicerade geometriska modeller (Ferlinz 1976).

Den första publicerade studien av cirkulationen med hjälp av radionuklider kom 1927 av Blumgart och Weiss, som mätte cirkulationstider med hjälp av radongas och en modifierad dimkammare som detektor. Under det senaste decenniet har stora framsteg gjorts inom den kardiovaskulära diagnostiken med hjälp av nya radionuklider, framför allt genom användning av $^{99}\text{Tc}^{\text{m}}$ och en betydande förbättring av mätapparaturen, numera gammakamera med minidator (Budinger & Rollo 1977; Bacharach et al. 1979).

Om blodet märks med en lämplig radionuklid, kan en bild av blodet i hjärtat registreras med gammakamera. Registreras flera bilder under hjärtcykeln, kan variationer i kammarstorleken bedömas, vilket benämns radionuklid-angiokardiografi (Schelbert et al. 1975). Med radionuklid-angiokardiografi bestämdes LVEF till en början enligt area-längd-metoden som vid röntgenologisk teknik (Strauss et al. 1971). Senare övergick man till att mäta förändringar i räknehastighet över kammaren under hjärtcykeln, vilka beror på volymsförändringar (Parker et al. 1972; Secker-Walker et al. 1973). Radionuklid-angiokardiografi kan utföras med två olika tekniker, vilka ofta kombineras, nämligen som första-passage-

undersökning eller som jämviktsundersökning. Vid första-passageundersökning kan några få hjärtslag analyseras under radionuklidens första passage genom kamrarna efter en bolusinjektion (Van Dyke et al. 1972; Steele et al. 1976). Vid första-passageundersökningen kan även ett mått på hjärtminutvolym och pulmonell blodvolym erhållas (Van Dyke et al. 1972; Rerych et al. 1978). Vid jämviktsundersökning fås radionukliden att stanna intravasalt och efter fullständig blandning i blodvolymen, då jämvikt inträtt, kan räknehastighetsförändringarna, d.v.s. blodvolymförändringarna, i kamrarna under hjärtcykeln mätas (Strauss et al. 1971; Secker-Walker et al. 1973; Maddahi et al. 1979). Fördelen med radionuklid-angiokardiografi är att inget antagande om kammarens geometri erfordras, vilket är av stort värde, speciellt för bedömning av höger kammare, men också då regionala förändringar föreligger i vänster kammarvägg, vilket oftast medför abnorm väggörslighet. Detta förekommer ofta vid ischemisk hjärtsjukdom. Ytterligare fördelar är att upprepade mätningar utan svårighet kan utföras under lång tid, speciellt med jämviktstekniken. Dessutom kan undersökning utföras under arbete (Borer et al. 1977; Rerych et al. 1978). En nackdel är att man också registrerar pulser som ej härstammar från den undersökta kammaren, s.k. bakgrundsaktivitet. Då detta bakgrundsproblem kan lösas på olika sätt med olika databearbetningsprogram, kan det erhållna ejektionsfraktionsvärdet variera något. Ett eget referensmaterial är därför nödvändigt. God överensstämmelse mellan radionuklid-angiokardiografi och röntgenologisk metodik för bestämning av ejektionsfraktionen har rapporterats (Folland et al. 1977; Ashburn et al. 1978; Sorensen et al. 1979).

Radionuklid-angiokardiografins fördelar och nackdelar som hjälpmedel i den kardiovaskulära diagnostiken måste dock ytterligare undersökas genom att jämföra den med andra väl beprövade metoder för bedömning av hjärtats funktion.

Undersökningens syften:

Denna undersöknings syften har varit:

1. att finna en lämplig metod för märkning av blodpoolen med $^{99}\text{Tc}^m$, för att kunna utföra upprepade mätningar av ejektionsfraktionen med radionuklid-angiokardiografi med jämviktsteknik;
2. att analysera reproducerbarheten vid bestämningar av ejektionsfraktionen med radionuklid-angiokardiografi;
3. att erhålla referensvärden för LVEF och RVEF i vila och under arbete;
4. att jämföra första-passagetekniken med jämviktstekniken för bestämning av RVEF med radionuklid-angiokardiografi;
5. att relatera RVEF till med kateteriseringsteknik samtidigt erhållna hemodynamiska variabler i vila och under arbete hos patienter med pulmonell hypertension;
6. att relatera LVEF till med kateteriseringsteknik samtidigt erhållna hemodynamiska variabler i vila och under arbete hos patienter med:
 - A. Myokardinfarkt
 - B. Koronarinsufficiens
 - C. Pulmonell hypertension.

MATERIAL

Referensgrupp

Referensgruppen bestod av 18 friska individer, varav två kvinnor. Fem läkare vid avdelningen deltog i referensgruppen. De övriga 13 individerna utgjordes av utredningsfall som remitterats till Kliniskt Fysiologiska Avdelningen, Malmö Allmänna Sjukhus, för undersökning avseende okarakteristiska bröstbesvär. Vid den slutliga bedömningen befanns alla med stor sannolikhet vara hjärt- och lungfriska. Aldern varierade från 18 till 60 år.

Patienter

I denna studie ingick 98 patienter, varav 15 kvinnor i åldern 18-73 år, med olika hjärt-lungsjukdomar. Patienterna var remitterade till Kliniskt Fysiologiska Avdelningen för undersökning av hjärtfunktionen. Efter muntlig information gav alla patienterna sitt tillstånd till undersökningens utförande. Alla patienterna hade sinusrytm.

METODER

1. Radionuklid-angiokardiografi

A. Utrustning

Mätningarna utfördes med en gammakamera (General Electric, Radikamera II). Energifönstret för $^{99}\text{Tc}^m$ och ^{133}Xe var $140 \text{ keV} \pm 15\%$ respektive $81 \text{ keV} \pm 15\%$. En "general purpose" parallellhålskollimator med diametern 26 cm användes. Gammakameran var ansluten till ett NUKAB-2530 system uppbyggt kring en PDP8/E-dator (Digital Equipment Corporation, U.S.A.). Vid alla undersökningarna registrerades signaler från gammakameran och R-vågssignaler från elektrokardiogrammet i "list mode" (64 x 64 matris). Med hjälp av en s.k. "hardware zoom" användes vid jämviktsundersökningen endast de centrala två tredjedelarna av kamerans synfält. Räknehastigheten vid första-passageundersökningarna var omkring $30\,000 \text{ s}^{-1}$. Vid jämviktsundersökningen var räknehastigheten omkring

16 000 s⁻¹. Ingen korrektion gjordes för dödtidsförlusterna, som ej översteg 5%. Varje vecka under hela undersökningsperioden utförde Radiofysikavdelningen vid Allmänna Sjukhuset i Malmö kontroller av gammakamerasystemet.

B. Positionering

Alla individer undersöktes i liggande ställning. Vid första-passageundersökningen placerades gammakameran 30° snett framifrån höger (RAO 30°).

Vid jämviktsundersökningen placerades gammakameran snett framifrån vänster (LAO). Den kameravinkel som bäst skiljde kamrarna åt användes, d.v.s. där kammarseptum syntes bäst på bilden. Denna vinkel var oftast LAO 30°. För att minska överlagringen av kammare och förmak vinklades kameran cirka 15° mot fotändan.

C. Första-passageundersökning

En central venkateter med spetsen i vena cava superior användes. Radionukliden, ⁹⁹Tc^m-pereteknetat eller ¹³³Xe-gas i fysiologisk koksaltlösning, i en volym mindre än 1 respektive 3 ml, placerades i en förlängningskateter, vars volym var 3 ml. Vid injektionen sköljdes radionukliden snabbt in i vena cava superior med 20 ml fysiologisk koksaltlösning. Pulserna från gammakameran och R-vågssignaler från elektrokardiogrammet registrerades i "list mode" tills radionukliden hade passerat vänster kammare, vilket kontrollerades med hjälp av gammakamerans minnesoscilloskop.

D. Jämviktsundersökning

När blodvolymen märkts med ⁹⁹Tc^m, insamlades vid varje registrering 1.6 milj. pulser, d.v.s. vad som rymdes på ett skivminne. Med använd aktivitet motsvarade detta en insamlingstid på 2-5 minuter.

E. Datarekonstruktion och bearbetning

1. Första-passagetekniken: Insamlade "list mode" data rekonstruerades till en dynamisk sekvens av 40 ms bilder. Då pulsfrekvensen översteg 125 min⁻¹, gjordes dock rekonstruktionen i 20 ms bilder. Ett preliminärt område, s.k. "region of interest", i fortsättningen benämnt region, motsvarande höger eller vänster

kammare definierades med hjälp av en ljuspenna på TV-monitors bild. Ur tid/räknehastighetskurvorna från dessa regioner utvaldes systoliska och diastoliska punkter i några hjärtslag. De till de diastoliska punkterna svarande 40 ms bilderna adderades till en diastolisk bild. På motsvarande sätt skapades en systolisk bild. Dessa två summerade bilder användes för att bättre definiera klaffplanen genom att på en TV-monitor växelvis visa dem som en film. Genom att subtrahera den systoliska bilden (S) från den diastoliska (D) erhöles en ny speciell bild, där kamrarnas slagvolym (där D-S gav ett positivt värde) och förmakens fyllnadsvolym (där D-S gav ett negativt värde) samtidigt visades. Även denna bild användes som hjälp för att bättre definiera klaffplanen. En slutgiltig slutdiastolisk kammarregion inritades därefter manuellt. Automatiskt erhöles en bakgrundsregion som var två bildelement bred och två bildelement utanför kammarregionen men ej tilläts innehålla hjärtrum eller stora kärl. På den nedåtsluttande delen av tid/räknehastighetskurvan utvaldes 2-4 slag under högerkammarpassagen och 4-8 slag under vänsterkammarpassagen som rekonstruerades till ett medelhjärtslag (Folland et al. 1977) genom att synkront addera sekventiella 40 ms bilder - vid pulsfrekvens $> 125 \text{ min}^{-1}$, 20 ms bilder - startande 200 ms före R-vågssignalen. Tid/räknehastighetskurvor under detta medelhjärtslag framställdes från kammarregionen och bakgrundsregionen. Bakgrundskurvan normaliserades, d.v.s. multiplicerades med kvoten mellan arean för kammarregionen och arean för bakgrundsregionen, varefter den subtraherades från kammarkurvan. Därefter uträknades ejektionsfraktionen som:

$$\frac{(\text{slutdiastolisk räknehastighet} - \text{slutsystolisk räknehastighet})}{\text{slutdiastolisk räknehastighet}}.$$

Ejektionsfraktionen angavs i procent.

2. Jämviktstekniken: Av de insamlade R-R-intervallen utvaldes de vars duration låg inom cirka $\pm 10\%$ av medeldurationen. Dessa R-R-intervall adderades synkront i löpande 40 ms bilder - vid pulsfrekvens $> 125 \text{ min}^{-1}$, 20 ms bilder - med start 200 ms före R-vågssignalen. En preliminär kammarregion utritades. Ur tid/räknehastighetskurvan från denna region utvaldes systoliska och diastoliska punkter, varefter motsvarande bilder användes för att definiera klaffplanen på samma sätt som vid första-passageundersökningen. Den slutgiltiga slutdiastoliska kammarregionen inritades på en speciell diastolisk bild som förstärkte hjärtkonturen. Denna bild erhöles genom att för varje bildelement i den diastoliska bilden beräkna kvadraten av förändringarna i antalet pulser i X- och Y-led. Den

då erhållna bilden var till stor hjälp för att bestämma kamrarnas begränsningar och därmed dess regioner. På detta sätt kunde såväl slutdiastolisk högerkammerregion som slutdiastolisk vänsterkammerregion definieras. Även då slutsystoliska höger- och vänsterkammerregioner användes, definierades dessa med hjälp av motsvarande behandling av den systoliska bilden. Automatiskt erhöles en bakgrundsregion som var två bildelement bred och två bildelement utanför den slutdiastoliska vänsterkammerregionen men ej tilläts omfatta hjärtrum eller stora kärl, d.v.s. omfattande bara laterala och inferiora delen utanför vänster kammars region. Tid/räknehastighetskurvor framställdes sedan för kammar- och bakgrundsregionerna. Bakgrundskurvan normaliserades och subtraherades sedan från kammarkurvan, varefter LVEF uträknades som:

$$\frac{(\text{slutdiastolisk räknehastighet} - \text{slutsystolisk räknehastighet})}{\text{slutdiastolisk räknehastighet}}.$$

Då diastolisk och systolisk region användes, gjordes normaliserad bakgrunds-subtraktion från respektive tid/räknehastighetskurva. LVEF eller RVEF uträknades som ovan genom att den slutdiastoliska och slutsystoliska räknehastigheten erhöles från den bakgrundssubtraherade tid/räknehastighetskurvan för den diastoliska respektive systoliska regionen.

F. Stråldoser

I Tabell 1 anges såväl den i hela kroppen i medeltal absorberade dosen som den effektiva dosekvivalenten för de i denna undersökning använda radionukliderna $^{99}\text{Tc}^m$ och ^{133}Xe , dels per MBq (Johansson et al. 1981) och dels per undersökning med angiven aktivitet.

2. Kateteriseringsteknik

Arteriella tryck och blodprover erhöles från en med Seldinger-teknik inlagd kateter (PE 160) i arteria brachialis. En liknande kateter eller en hjärtkateter inlades perkutant via mediala armbågsvenor till vena cava superior, högerhjärtat eller arteria pulmonalis med hjälp av genomlysning. Det diastoliska trycket i arteria pulmonalis eller medeltrycket i "wedge"-position (pulmonary capillary venous mean pressure) användes som mått på vänster kammars fyllnadstryck (LVFP) (Falicov & Resnekov 1970; Jenkins et al. 1970). Trycken registrerades med standardutrustning (tryckgivare 746 och Mingograf

Tabell 1

STRÅLDOSER

<u>Radionuklid</u>	<u>Absorberad medelhelkroppsdos</u>	<u>Effektiv dosekvivalent</u>
$^{99}\text{Tc}^{\text{m}}$ -perteknetat 350 MBq	0.0038 mGy/MBq 1.33 mGy	0.011 mSv/MBq 3.85 mSv
$^{99}\text{Tc}^{\text{m}}$ -märkta erythrocyter 500 MBq	0.0047 mGy/MBq 2.35 mGy	0.0070 mSv/MBq 3.50 mSv
$^{133}\text{Xenon}$ i fysiologisk koksalt 750 MBq	0.00024 mGy/MBq 0.18 mGy	0.00043 mSv/MBq 0.32 mSv

81, Siemens-Elema AB, Stockholm). Nollnivån var 5 cm under angulus sterni. Medeltryck erhöjls med elektrisk dämpning. Hjärtminutvolymen mättes med färgspädningsteknik (bromsulphalein, Wassén 1956). Vänster kammares slagarbete (SWI), joule/slag/m², uträknades som (medelartärtrycket - LVFP i mm Hg) x slagvolymsindex i ml/m² x 1.33 x 10⁻⁴. Resistensindex i lungkretsloppet uträknades som (medeltrycket i arteria pulmonalis - LVFP i mm Hg)/hjärtminutvolymindex i l/min/m².

Reproducerbarheten för slagvolymsindex (SI) mättes som metodfelet vid dubbelbestämning i vila hos 22 patienter. Metodfelet var 2.0 ml/m² och medelvärde av SI var 43.1 ml/m², vilket gav en variationskoefficient på 4.6%.

Vänster kammares slutdiastoliska volym (LVEDVI) i ml/m² kunde lätt uträknas, då SI och LVEF var kända (LVEDVI = 100 x SI/LVEF). Vänster kammares slutsystoliska volym (LVESVI) erhöjls genom att subtrahera SI från LVEDVI.

Referensvärden erhöjls från Malmberg (1965). Skillnaden i nollnivå mellan 5 cm under angulus sterni, som användes vid dessa undersökningar, och mitthorakalhöjd, som användes av Malmberg motsvarar cirka 3 mm Hg. Referensvärdena är därför korrigerade i motsvarande grad.

3. Statistik

Vanliga statistiska metoder beskrivna av Bradford Hill (1977) användes. Medelvärde ± 1 standarddeviation presenteras i den fortsatta redovisningen. En sannolikhet, P < 0.05, ansågs signifikant. Metodfelet (e) vid dubbelbestämningar uträknades enligt Dahlberg (1948):

$$e = \sqrt{\frac{\sum d^2}{2n}}$$

där $\sum d^2$ är summan av kvadraten på skillnaderna och n är antalet dubbelbestämningar.

RESULTAT OCH DISKUSSION

1. Märkning av blodvolymen med $^{99}\text{Tc}^m$

För att kunna göra upprepade bestämningar av ejektionsfraktionen med radionuklid-angiokardiografi med jämviktsteknik fordras att radionukliden under mättiden stannar intravasalt. De tillgängliga metoderna för blodvolymsmärkning med $^{99}\text{Tc}^m$ innefattade in vitro märkning till humant albumin (Thrall et al. 1978) eller till röda blodkroppar (Smith & Richards 1976) och in vivo märkning till röda blodkroppar (Pavel et al. 1977). Dessa märkningsmetoder jämfördes i uppsats I.

Aktivitetskoncentrationen av $^{99}\text{Tc}^m$ i helblod i relation till given dos per kg kroppsvikt mättes under två timmar hos 25 patienter. Även förhållandet mellan nettoräknehastigheten i vänster kammare i relation till räknehastigheten i ett bakgrundsområde mättes. Resultaten visade att vid märkning till albumin var aktivitetskoncentrationen av $^{99}\text{Tc}^m$ i helblod i relation till given dos signifikant lägre redan 15 minuter efter injektionen jämfört med erythrocytmärkningarna. Nettoräknehastigheten över vänster kammare i relation till räknehastigheten över bakgrunden var signifikant lägre efter 90 minuter men väsentligen lika efter 30 minuter jämfört med erythrocytmärkningarna. Då erythrocytmärkningarna jämfördes, uppvisade in vitro metoden initialt högre aktivitetskoncentration av $^{99}\text{Tc}^m$ i helblod, men efter 15 minuter förelåg ingen signifikant skillnad. Med båda erythrocytmärkningsmetoderna var försvinnandet av $^{99}\text{Tc}^m$ från blodbanan mycket långsamt (cirka 6% per timme efter korrektion för det fysikaliska sönderfallet). Nettoräknehastigheten över vänster kammare i relation till räknehastigheten över bakgrunden skiljde sig inte 30 eller 90 minuter efter injektionen.

Slutsatsen av undersökningen blev att blodvolymsmärkning med $^{99}\text{Tc}^m$ bör ske med en av erythrocytmärkningsmetoderna. Med in vitro märkning av erythrocyterna enligt Smith och Richards (1976) blev den $^{99}\text{Tc}^m$ -märkta erythrocytvolymen som sedan injicerades cirka 4 ml. Med in vivo märkning av erythrocyterna kunde volymen av $^{99}\text{Tc}^m$ -perteknetat hållas liten, < 1 ml. Dessa skillnader i volymer är oväsentliga för utförande av radionuklid-angiokardiografi med jämviktsteknik. Skall undersökningen kombineras med första-passageteknik, vilket ofta göres, är en kompakt radionuklidbolus viktig (Berger et al. 1979b).

Då in vivo märkningen var enklare att utföra, har denna metod använts för radionuklid-angiokardiografi med jämviktstekniken i övriga uppsatser (III, IV och V).

2. Reproducerbarhet

Reproducerbarheten vid radionuklid-angiokardiografi analyserades med dubbelbestämningar, varvid Dahlbergs formel för metodfel användes som mått på reproducerbarheten. I vila var durationen mellan dubbelbestämningarna mindre än 15 minuter. Under arbete gjordes den första registreringen efter 3-4 minuter, då arbetspulsen hade stabiliserats. Den andra registreringen påbörjades inom en minut efter den första.

Resultaten presenteras i Tabell 2.

A. RVEF i vila mätt med första-passageteknik med ^{133}Xe : Dubbelbestämningar hos 13 individer gav ett metodfel på 2.6 procentenheter.

B. RVEF i vila mätt med jämviktsteknik enligt Maddahi et al. (1979): Dubbelbestämningar hos 16 individer gav ett metodfel på 3.8 procentenheter.

Reproducerbarheten för bestämning av RVEF i vila var bättre om första-passagetekniken med ^{133}Xe användes än om jämviktstekniken användes.

C. LVEF i vila mätt med jämviktsteknik med en diastolisk kammarregion: Dubbelbestämningar utfördes på 17 individer. Hos 7 individer flyttades patienten och kameran mellan undersökningarna, varefter ny inställning gjordes. Hos de övriga 10 individerna skedde ingen kameraflyttning. Flyttningen påverkade inte metodfelet, som var 1.8 procentenheter (Tabell 2).

D. LVEF i vila mätt med jämviktsteknik med en diastolisk och en systolisk kammarregion: Dubbelbestämning utfördes hos 16 individer och metodfelet blev 2.6 procentenheter.

E. LVEF under arbete mätt med jämviktsteknik med en diastolisk kammarregion: Hos 13 individer utfördes 24 dubbelbestämningar på olika belastningar. Under lätt arbete, medelbelastning 43 W (variationsvidd 20-50 W) och medelpuls-

Tabell 2

Reproducerbarheten, mätt som metodeflet vid dubbelbestämningar, för bestämning av ejektionsfraktionen med radionuklid-angiokardiografi

Teknik	Jämviktsteknik										Första passage teknik
Undersökt kammare	Vänster kammare					Höger kammare					
Betingelser	A) Vila + kamera-flyttning	B) Vila ej kamera flyttning	A+B) Vila	C) Vila	D) Arbete ≤ 50 W	E) Arbete > 50 W	D+E) Arbete 25-150 W	F) Vila	G) Vila		
Val av "region of interest" D = diastolisk S = systolisk	D	D	D	S+D	D	D	D	S+D	D		
Antal dubbelbestämningar (n)	7	10	17	16	16	8	24	16	13		
Metodfel (e) $e = \sqrt{\sum d^2/2 n}$	1.9	1.8	1.8	2.6	2.9	3.3	3.0	3.8	2.6		
Medelvärdet ($\bar{M}$) av alla bestämningarna	48.0	45.6	46.6	53.0	51.0	66.2	56.1	44.6	45.2		
Variationskoefficient 100 x e/ $\bar{M}$	3.9	3.9	3.9	5.0	5.7	5.0	5.3	8.5	5.7		

$\sum d^2$ = kvadraten av summan av alla differenser vid dubbelbestämningar (Dahlberg 1948).

frekvens 93 min^{-1} (variationsvidd $70\text{--}115 \text{ min}^{-1}$), var metodfelet 2.9 procentenheter. Under måttligt tungt arbete, medelbelastning 103 W (variationsvidd $75\text{--}150 \text{ W}$) och medelpulsfrekvens 123 min^{-1} (variationsvidd $84\text{--}155 \text{ min}^{-1}$), var metodfelet 3.3 procentenheter. Sammantaget var metodfelet under arbete 3.0 procentenheter (Tabell 2).

Ingen signifikant skillnad förelåg mellan den första och den andra bestämningen avseende ejektionsfraktionen eller pulsfrekvensen i samtliga ovanstående bestämningar i vila eller sammantaget under arbete.

Vid bestämning av LVEF i vila med jämviktsteknik var reproducerbarheten bäst då en slutdiastolisk vänsterkamarregion användes. Då en diastolisk och en systolisk vänsterkamarregion användes, var det svårare att säkert definiera den systoliska regionen, ju mindre det systoliska området var, d.v.s. ju högre LVEF var. Vid låga LVEF blev skillnaden mellan diastolisk och systolisk region allt mindre. Då den systoliska vänsterkamarvolymen under arbete normalt minskar, kunde inte en förbättring av reproducerbarheten vid användning av en diastolisk och en systolisk vänsterkamarregion för uträkning av LVEF förväntas under arbete. Då förändringar i LVEF skulle studeras, uträknades därför LVEF i de fortsatta undersökningarna endast med en diastolisk vänsterkamarregion.

Under arbete blev reproducerbarheten för LVEF mätt med en diastolisk kammarregion något sämre än i vila. Metodfelen var 3.0 respektive 1.8 procentenheter, vilket motsvaras av en variationskoefficient på 5.3% respektive 3.9% (Tabell 2).

3. Referensvärden för ejektionsfraktionen mätt med radionuklid-angiokardiografi

A. Höger kammars ejektionsfraktion

Referensvärden för RVEF mätt med första-passageteknik i vila erhöles från en referensgrupp på 17 individer, varav två kvinnor, med en medelålder av 40 år och en variationsvidd på 18–60 år. RVEF var i medeltal $49 \pm 5\%$ med en variationsvidd på 42–61% (Tabell 3).

Tabell 3

Referensvärden för ejektionsfraktionen i vila och under arbete bestämd med
radionuklid-angiokardiografi (medelvärde $\pm$ standarddeviation)

<u>Jämviktsteknik</u>	<u>Vila</u>	<u>50 W</u>	<u>100 W</u>	<u>150 W</u>	<u>Vila 10 min efter arbete</u>
LVEF %	56 $\pm$ 8	61 $\pm$ 8	67 $\pm$ 9	71 $\pm$ 8	59 $\pm$ 8
RVEF %	43 $\pm$ 5	49 $\pm$ 6	55 $\pm$ 6	53 $\pm$ 6	44 $\pm$ 7
Puls min ⁻¹	69 $\pm$ 10	101 $\pm$ 10	124 $\pm$ 8	153 $\pm$ 9	85 $\pm$ 12
n	12	12	10	9	11
<u>Första-passage- teknik</u>	<u>Vila</u>	<u>50 W</u>			
RVEF %	49 $\pm$ 5	53 $\pm$ 2			
Puls min ⁻¹	68 $\pm$ 11	108 $\pm$ 12			
n	17	5			

Hos fem friska individer, medelålder 39 år och variationsvidd 29-56 år, mättes RVEF med första-passagetekniken i vila och under lätt liggande arbete, 50 W. I vila var RVEF i medeltal $50 \pm 2\%$, variationsvidd 48-54%. Under arbete ökade RVEF till $53 \pm 2\%$, variationsvidd 51-55%. Ökningen var i medeltal 3 procentenheter, variationsvidd 0-7 procentenheter.

Referensvärden för RVEF mätt med radionuklid-angiokardiografi med jämviktsteknik erhöles från en referensgrupp på 12 individer, varav två kvinnor. Medelåldern var 38 år, variationsvidd 18-51 år. Dessa undersöktes i vila och under liggande arbete med cykelergometer. Registreringarna under arbete påbörjades då pulsen stabiliserats, d.v.s. efter 3-4 minuter på varje ny belastning. Resultaten framgår av Tabell 3. RVEF i vila var i medeltal $43 \pm 5\%$ med en variationsvidd på 37-53%. Hos alla individer ökade RVEF under arbete.

Tobinik et al. (1978), Johnson et al. (1979) och Berger et al. (1979a) har rapporterat referensvärden för RVEF mätt med första-passageteknik i vila och/eller under arbete hos friska individer i åldrarna 17-73 år. Inget åldersberoende förelåg i vila och inte heller tycktes något sådant föreligga i förändringen av RVEF under arbete. Ingen av de rapporterade friska individerna i åldern 25-69 år sjönk i RVEF vid sittande arbete.

Slutsky et al. (1980), som använde jämviktstekniken med en diastolisk högerkammerregion för att beräkna RVEF i vila och under liggande arbete hos 20 friska individer i åldern 24-52 år, rapporterade en ökning i RVEF från $49 \pm 10\%$ i vila till $64 \pm 12\%$ under arbete. Inte hos någon individ sjönk RVEF under arbete.

B. Vänster kammars ejektionsfraktion

Referensvärden för LVEF mätt med radionuklid-angiokardiografi med jämviktsteknik erhöles från samma individer som ovan, då RVEF bestämdes med jämviktsteknik. LVEF var i vila $56 \pm 8\%$ med en variationsvidd på 44-71%. Under lätt arbete, 50 W, ökade LVEF i medeltal 5.5 ± 3.2 procentenheter, variationsvidd -1 till 11 procentenheter. En sänkning av LVEF med mer än en procentenhet tolkades som en patologisk LVEF-reaktion under lätt arbete. På högsta belastningen ökade alla individerna sin LVEF jämfört med i vila, i medeltal 14 ± 4 procentenheter, variationsvidd 10-21 procentenheter.

Flera studier (Borer et al. 1978; Pfisterer et al. 1979; Sorensen et al. 1980) har hos sammanlagt 60 friska individer i åldern 19-63 år rapporterat en ökning av LVEF under liggande arbete hos samtliga. Något åldersberoende rapporterades inte.

Port et al. (1980) studerade LVEF i vila och under sittande arbete med första-passagetekniken i en referensgrupp på 77 individer i åldern 20-95 år. LVEF i vila befanns ej vara beroende av åldern. Under arbete däremot sjönk LVEF med tilltagande ålder, och ökningen av LVEF under arbete var omvänt relaterad till åldern. Hos flertalet individer över 60 år sjönk LVEF under arbete. En ökande frekvens av segmentell störning av vänster kammars väggrörlighet tillkom också under arbete hos individerna över 60 år. Detta antyder en hög incidens av asymptomatisk ischemisk hjärtsjukdom, vilket diskuteras av Weisfeldt (1980) och vilket är förenligt med obduktionsfynd (White et al. 1950). Port och medarbetare (Upton et al. 1980) studerade med samma metodik 25 patienter med påvisad koronarsjukdom under arbete vid en belastning då vare sig smärta eller EKG-förändringar förelåg. Hos dessa patienter var förändringen av LVEF under arbete abnorm hos 72%. Samtidigt utvecklades segmentell störning i vänster kammars väggrörlighet under arbete hos 56% av patienterna. Under tyngre arbete uppvisade alla patienterna ST-sänkningar i EKG och alla hade då abnorma förändringar i LVEF och i vänster kammars väggrörlighet. Rapporten av Upton et al. (1980) tyder på att asymptomatisk ischemisk hjärtsjukdom kan vara en mycket starkt bidragande orsak hos äldre individer till de fynd Port et al. (1980) rapporterade. Det får därför anstå till kommande, helst longitudinella, undersökningar att fastställa om ett säkert åldersberoende föreligger i ejektionsfraktionens förändring under liggande arbete.

4. Jämförelse mellan första-passageteknik och jämviktsteknik för bestämning av höger kammars ejektionsfraktion med radionuklid-angiokardiografi

Med radionuklid-angiokardiografi kan RVEF bestämmas med såväl första-passageteknik som jämviktsteknik. Steele et al. (1976) har rapporterat överensstämmelse mellan första-passagetekniken och röntgenologisk metodik för bestämning av RVEF. Korrelationskoefficienten var 0.80 vid undersökning av 43 patienter. Jämviktstekniken för bestämning av RVEF beskrevs först av Maddahi et al. (1979), som fann god överensstämmelse gentemot första-passagetekniken. Vid

upprepade bestämningar med första-passagetekniken fordras upprepade bolusinjektioner, vilket medför högre stråldos och problem med ökad bakgrund, om inte en radionuklid med kort biologisk halveringstid används.

I uppsats II användes första-passagetekniken för att bestämma RVEF, varvid två radionuklider, $^{99}\text{Tc}^m$ och ^{133}Xe jämfördes. ^{133}Xe har kort biologisk halveringstid, någon minut, på grund av snabb utvädring via lungorna. Korrelationen mellan $^{99}\text{Tc}^m$ och ^{133}Xe vid bestämning av RVEF var god, då korrelationskoefficienten var 0.88 och residualspridningen var 4.7 procentenheter hos 26 patienter. Reproducerbarheten vid dubbelbestämningar var god, då metodfelet var 2.6 procentenheter.

I uppsats III jämfördes första-passagetekniken och jämviktstekniken för bestämning av RVEF hos 10 patienter med pulmonell hypertension. Bestämningar gjordes i vila och under arbete två gånger med en timmes vilopaus emellan. Vid den första undersökningen bestämdes RVEF med första-passagetekniken med ^{133}Xe som spårämne i vila och med $^{99}\text{Tc}^m$ som spårämne under arbete. Vid den andra undersökningen bestämdes RVEF med jämviktstekniken. En god överensstämmelse mellan första-passage- och jämviktstekniken erhöles med en korrelationskoefficient i vila och under arbete på 0.86 respektive 0.91.

5. Relation mellan höger kammars ejektionsfraktion och hemodynamiska variabler

I uppsats III studerades även relationen mellan RVEF, mätt med radionuklidangiokardiografi, och hemodynamiska variabler, samtidigt erhållna genom kateterisering. Det förelåg en god negativ korrelation mellan RVEF och graden av pulmonell hypertension mätt som trycket i arteria pulmonalis eller som vaskulärt resistensindex i lungkretsloppet. Korrelationskoefficienterna var -0.53 till -0.88. Den bästa korrelationen förelåg då första-passagetekniken användes för RVEF-bestämning. I vila hade en patient högt fyllnadstryck i höger kammare, mätt som medeltrycket i höger förmak, och denna patient hade även låg RVEF i vila. Under arbete hade ytterligare fem patienter högt fyllnadstryck i höger kammare och alla dessa hade samtidigt låg eller sjunkande RVEF vid arbete.

De fem patienter som kliniskt hade haft tecken på högersvikt hade låg eller sjunkande RVEF vid arbete.

6. Relation mellan vänster kammarens ejektionsfraktion och hemodynamiska variabler vid olika sjukdomstillstånd

Vänster kammarens ejektionsfraktions värde för bedömning av kammarfunktionen jämfördes med samtidigt registrerade centrala tryck och flöden i vila och under arbete hos patienter med myokardinfarkt, med koronarinsufficiens och med pulmonell hypertension (uppsats IV, V och III). LVEF mättes med radionuklidangiokardiografi med jämviktsteknik.

A. Myokardinfarkt

I uppsats IV undersöktes 22 patienter på i genomsnitt elfte dagen efter sin första transmurala myokardinfarkt. Fem patienter, som i vila hade patologiskt för högt fyllnadstryck i vänster kammare (LVFP) mätt som diastoliskt tryck i arteria pulmonalis, hade patologiskt låg LVEF. Fyra patienter, som under arbete hade patologiskt högt LVFP, hade patologiskt låg LVEF eller patologisk LVEF-reaktion vid arbete. Patologiskt låg LVEF i vila förelåg hos ytterligare tre patienter som hade normalt LVFP. Även under arbete var LVEF patologiskt låg hos åtta patienter, vars LVFP var inom normalvariationen. Två av dessa senare patienter hade låg slagvolym i såväl vila som under arbete, vilket tydde på vänsterkamardysfunktion. LVEF-mätningen syntes således känsligare än LVFP-mätningen när det gällde att avslöja vänsterkamardysfunktionen. Det förelåg även en signifikant negativ korrelation mellan LVFP och LVEF i såväl vila som under arbete.

Om LVEF-mätningen jämfördes med såväl flödes- som tryckmätningen för bedömning av vänsterkammarfunktionen, befanns LVEF vara lika känslig när det gällde att avslöja vänsterkamardysfunktion.

B. Koronarinsufficiens

I uppsats V undersöktes 10 patienter med koronarinsufficiens i vila och under arbete. Alla hade normal central hemodynamik och normal LVEF i vila. Under arbete fick alla patienterna ont i bröstet, patologiskt högt LVFP och patologisk sänkning av LVEF. Hos nio patienter sjönk slagvolymen under arbete. Efter arbete återgick såväl LVFP som LVEF mot vilovärdet. LVEF-mätningen

avslöjade vänsterkamardysfunktion under ansträngningsangina lika ofta som kateteriseringsresultaten. Ingen signifikant korrelation förelåg mellan förändringarna i LVFP och förändringarna i LVEF.

C. Pulmonell hypertension

I uppsats III undersöktes 10 patienter med pulmonell hypertension. Två patienter hade även arteriell hypertension, varav den ena hade EKG-tecken på vänsterkammарhypertrofi men för övrigt hade ingen kliniska hållpunkter för vänsterkammarsjukdom eller vänsterkammарpåverkan. I vila hade alla normalt LVFP, mätt som medeltrycket i "wedge"-läge i arteria pulmonalis, medan två hade låg LVEF. Under arbete registrerades hos tre patienter patologiskt högt LVFP. Dessa tre patienter hade låg LVEF eller sänkning av LVEF vid arbete. Ytterligare två patienter hade sänkning av LVEF utan att LVFP var förhöjt under arbete.

Vid radionuklid-angiokardiografi registreras förändringar i räknehastigheten, vilka motsvaras av volymsförändringar. Ejektionsfraktionen kan då lätt bestämmas utan att något antagande om kammargeometrin behöver göras. Helt fri från geometriska överväganden är metoden dock inte, eftersom den linjära relationen mellan räknehastighet och absolut volym påverkas av den attenuering, absorption, som sker i kamrarnas blod. Detta gäller framför allt vid mycket dilaterade kamrar, vars räknehastighet (volym) då underskattas. Detta kan medföra ett fel i beräkningen av ejektionsfraktionen vid dilaterade kamrar på upp till 10% enligt Buddemeyer et al. (1979).

Radionuklid-angiokardiografi kan utföras med såväl första-passageteknik som jämviktsteknik, vilka ofta kombineras. Då kan såväl RVEF som LVEF bestämmas vid upprepade mätningar under några timmar, varvid olika interventioner kan ske, utan att individens erhållna stråldos ökas. Den effektiva dosekvivalent en individ får om erythrocyterna märkes med 500 MBq $^{99}\text{Tc}^{\text{m}}$ -pereteknetat är 3.5 mSv (Tabell 1). Motsvarande effektiv dosekvivalent vid en vänsterkammerangiokardiografi beräknas vara cirka 45 mSv (Monika Gustavsson, personligt meddelande).

1. Höger kammars ejektionsfraktion

Med första-passagetekniken kan höger kammare lättare avgränsas och bakgrundsproblemen minimeras. Genom att positionera kameran snett framifrån höger kan höger kammare lätt friprojiceras. Denna projektion är bara användbar när ingen radionuklid finns i vänsterhjärtat. Om upprepade första-passageundersökningar skall göras, fordras upprepade injektioner, vilket ger högre stråldos till patienten och besvär med bakgrunden. Med jämviktstekniken kan upprepade mätningar lätt göras, samtidigt som LVEF också kan mätas. Första-passage-teknikens reproducerbarhet var bättre än jämviktsteknikens. Första-passage-tekniken korrelerade också bättre till samtidigt mätta kateteriseringsvariabler hos patienter med pulmonell hypertension. RVEF-bestämning med första-passage-tekniken föreföll därför mer tillförlitlig än med jämviktstekniken. Om ^{133}Xe används som spårämne, kan cirka 10 första-passagemätningar av RVEF göras, innan patienten erhåller en lika stor stråldos som vid jämviktstekniken.

I referensgrupperna skiljde sig medelvärdena för RVEF mätt med första-passage-teknik, $49 \pm 5\%$, och med jämviktsteknik, $43 \pm 5\%$, signifikant, $P < 0.01$. Detta betingas sannolikt av svårigheten att friprojicera höger kammare, när jämviktstekniken användes. Om någon del av höger förmak ingår i den systoliska högerkammerregionen, leder detta till en lägre RVEF. Maddahi et al. (1979) erhöll lägre värden för RVEF med jämviktstekniken, $46 \pm 12\%$, jämfört med första-passagetekniken, $48 \pm 13\%$ i en patientgrupp.

Om RVEF och kateteriseringsvariablerna jämfördes hos patienter med pulmonell hypertension, befanns alla patienter med kateteriseringsresultat tydande på högerkammardysfunktion, också ha abnorm RVEF. Även hos alla patienter med anamnes på tidigare högerkammersvikt kunde abnorm RVEF uppmätas. Oftast kunde denna högerkammardysfunktion i form av högt medeltryck i höger förmak och låg eller sjunkande RVEF endast registreras under arbete.

Även om korrelationen mellan RVEF och trycket i arteria pulmonalis var god, kunde RVEF inte användas för att uppskatta den pulmonella hypertensionen, eftersom några patienter med pulmonell hypertension hade normal RVEF.

RVEF syntes emellertid vara ett tillförlitligt mått på högerkamarfunktionen. Diagnosen pulmonell hypertension med högerkammersvikt är svår att ställa vid kronisk lungsjukdom, eftersom insufficienssymptomen från hjärta och lungor ofta är svåra att skilja (Piemme 1972). Bestämning av RVEF hos patienter med kronisk lungsjukdom torde därför vara av kliniskt värde när det gäller att bedöma högerkammars funktion. Förbättring av RVEF vid behandling av patienter med kronisk obstruktiv lungsjukdom har påvisats med kronisk syrgasbehandling (Ellis et al. 1977) och med aminofyllin (Matthay et al. 1978), varför RVEF kan vara värdefull för uppföljning av behandling. Om RVEF har prognostiskt värde vid kronisk lungsjukdom får framtida undersökningar utvisa. Även vid ischemisk hjärtsjukdom har RVEF-påverkan rapporterats, vilket bör ha kliniskt värde. Vid akut inferior myokardinfarkt är RVEF ibland låg (Reduto et al. 1978), speciellt om högerkamarinfarkt föreligger (Tobinick et al. 1978) och vid proximal stenosis i höger koronarkärl var RVEF-reaktionen under arbete abnorm i cirka 75% av patienterna (Johnson et al. 1979).

2. Vänster kammare ejektionsfraktion

LVEF beräknades i denna sammanfattning med radionuklid-angiokardiografi med jämviktsteknik efter blodpoolsmärkning med $^{99}\text{Tc}^m$ till röda blodkroppar in vivo. En slutdiastolisk vänsterkamarregion användes vid beräkningen, eftersom denna uträkningsmetod visade sig ha bäst reproducerbarhet. LVEF beräknad på detta sätt ger lägre värden än då diastolisk och systolisk vänsterkamarregion eller röntgenologisk teknik används, men LVEF mätt med de olika metoderna korrelerar bra (Sorensen et al. 1979). Våra referensvärden för LVEF, $56 \pm 8\%$, är cirka 15% lägre än vad som anges för röntgenologisk teknik, $67 \pm 8\%$, (Kennedy et al. 1966). Den använda referensgruppen, som till huvuddelen bestod av patienter som efter noggrann undersökning ansågs vara hjärt- och lungfriska, utgör inte en idealisk normalgrupp. Värdena på ejektionsfraktionen kan i denna referensgrupp vara något litet förskjutna mot låga värden. Detta innebär emellertid att en skillnad mellan en patientgrupp och en idealisk normalgrupp inte överskattas med dessa referensvärden. Å andra sidan torde dessa referensvärden innebära en viss sänkning av metodens sensitivitet.

Vid samtidig jämförelse med kateteriseringsteknik befanns alla patienter (uppsats III, IV och V) med vänsterkamardysfunktion i vila, mätt som förhöjt LVFP, ha för låg LVEF. Även alla patienter som visade tecken på vänsterkamardysfunktion endast under arbete hade för låg eller sjunkande LVEF. Dessutom var LVEF abnorm i vila eller under arbete vid 11 av 44 samtidiga jämförelser hos patienter med myokardinfarkt (uppsats IV) samtidigt som LVFP var inom referensområdet. Då flera av dessa senare patienter hade andra tecken på möjlig vänsterkamardysfunktion som liten slagvolym och genomgången myokardinfarkt, bedömdes LVEF vara en mer sensitiv parameter än LVFP när det gällde att avslöja vänsterkamardysfunktion.

Vid samtidig mätning av LVEF med radionuklid-angiokardiografi och slagvolym med färgspädningsteknik kunde vänster kammare volym (LVEDVI och LVESVI) beräknas. Då LVEF, mätt med en diastolisk kammarregion gav något låga värden, medförde detta att kammarvolymerna uträknade på detta sätt blev något stora, jämfört med röntgenologisk beräkning. Det relativa metodfelet uttryckt som variationskoefficient (VK) för LVEDVI kan uträknas då motsvarande relativa metodfel är kända för SI och LVEF enligt formeln (Beers 1962):

$$VK_{LVEDVI} = \sqrt{VK_{SI}^2 + VK_{LVEF}^2}$$

Då VK för SI och LVEF i vila var 4.6% (metoder) och 3.9% (Tabell 2), blev VK för LVEDVI i vila 6.0%.

LVEF är ett mått på systolisk myokardfunktion och vänster kammars slutdiastoliska tryck, i denna sammanfattning uppskattad från medeltrycket i "wedge"-läge eller från det diastoliska trycket i arteria pulmonalis (LVFP), är ett mått på vänster kammars diastoliska egenskaper. Dessa två variabler behöver inte nödvändigtvis korrelera hos den enskilde patienten. I infarktgruppen (uppsats IV) förelåg en god korrelation mellan LVEF och LVFP i såväl vila som under arbete. Även förändringarna i LVEF och LVFP under arbete korrelerade till varandra. Detta var inte fallet i koronarinsufficiensgruppen (uppsats V). Denna skillnad i korrelation kan betingas av att LVEF och LVFP speglar olika aspekter av vänsterkammerfunktionen, och att dessa kan påverkas olika vid övergående ischemi och vid statisk myokardskada. Av Fig. 1 framgår också att patienter med

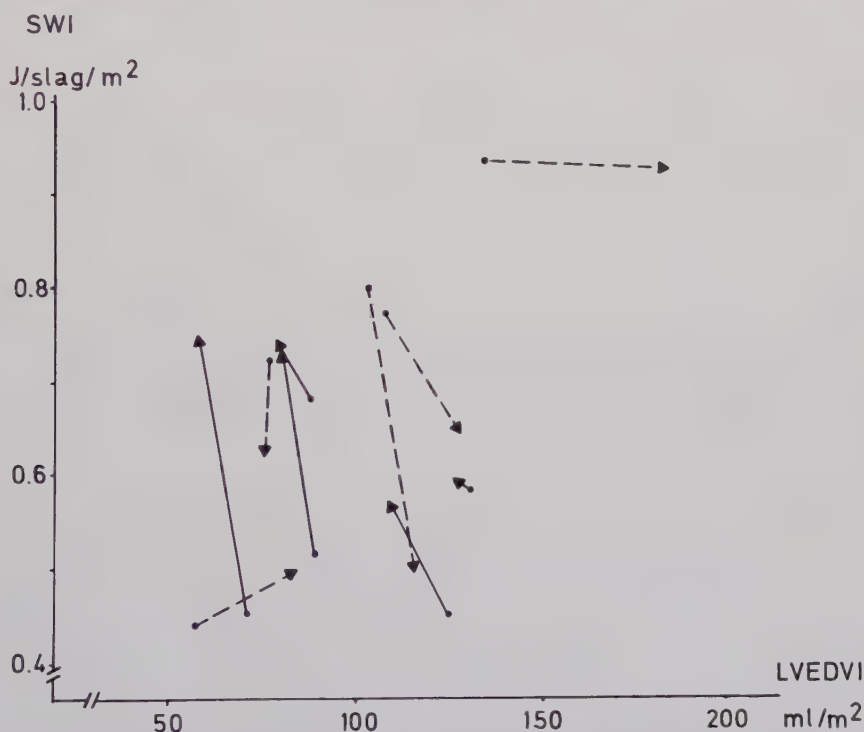


Fig. 1. Förändringarna i vänster kammars slagarbete (SWI) och vänster kammars slutdiastoliska volym (LVEDVI) från vila (●) till arbete (►) hos 5 patienter utan myokardinfarkt men med ansträngningsutlöst angina pectoris (-----) och hos 5 patienter med myokardinfarkt men utan besvär vid arbete (—).

myokardinfarkt och patienter med myokardischemi även kan bete sig olika avseende SWI och LVEDVI. Patienterna i Fig. 1 utgöres av de fem patienterna med angina pectoris men utan tidigare myokardinfarkt (uppsats V) samt de fem patienter med myokardinfarkt (uppsats IV), där det liggande arbetet ej avbröts på grund av besvär utan på grund av uppnådd maximal belastning, 60 W. Patienter med myokardinfarkt sjönk i LVEDVI och ökade i SWI, medan patienterna med angina pectoris tenderade att öka i LVEDVI och sjunka i SWI. Normala individer ökar i SWI under arbete (Malmborg 1965).

Hos patienter med ansträngningsangina (uppsats V) befanns den låga LVEF vid arbete orsakas framför allt av ökning av den systoliska vänsterkammарvolymen. Det höga LVFP under arbete var ibland förenat med en oförändrad eller t.o.m. minskad slutdiastolisk vänsterkammарvolym. Detta tyder på lägre diastolisk kammар-compliance vid ansträngningsangina än i vila.

Vid konstruktion av funktionskurvor för vänster kammare, s.k. Starling-kurvor, används ofta LVFP som mått på diastolisk tånjning (Katz 1977), eftersom det bättre måttet diastolisk vänsterkammарvolym ofta är svårtillgängligt.

Om radionuklid-angiokardiografi och kateteriseringsteknik används samtidigt, kan sådana funktionskurvor lättare konstrueras i såväl vila som arbete och mer uttömmande information om vänsterkammарfunktionen kan erhållas. Förändringar i slagvolym eller slagarbete hos vänster kammare utan samtidiga förändringar av slutdiastolisk kammарvolym (preload) och systoliskt kammар- eller artärtryck (afterload) innebär motsvarande förändringar i kontraktiliteten. Lämpliga framtida forskningsuppgifter kan vara att samla denna mer uttömmande information om hjärtfunktionen vid olika sjukdomstillstånd och vid olika interventioner.

Vänsterkammарdysfunktion i vila och under arbete kunde alltså påvisas med LVEF-mätning lika bra som med kateteriseringsteknik. För klinisk användning är därför LVEF-bestämning i vila eller under arbete värdefull för påvisande av dysfunktion hos patienter med myokardinfarkt, där även en kvantifiering kan göras. LVEF kan även användas i prognostiskt syfte efter myokardinfarkt (Feild et al. 1972; Rigo et al. 1974) men även vid kardiomyopati (Feild et al. 1973; Kreulen et al. 1973), ischemisk hjärtsjukdom och klaffsjukdom (Cohn et al. 1974; Nelson et al. 1975). Effekten av läkemedels inverkan på vänsterkammар-

funktionen kan studeras, t.ex. positiv effekt av digitalis (Vogel et al. 1977) eller negativ effekt av doxorubicin (Alexander et al. 1979). Mätning av LVEF-reaktionen under arbete är värdefull vid utredning av patienter med bröstsmärtor (Borer et al. 1977; Rerych et al. 1978; Upton et al. 1980) men även vid bedömning av aortainsufficiens (Borer et al. 1978).

SLUTSATSER

1. Blodpoolsmärkning av röda blodkroppar in vivo med $^{99}\text{Tc}^m$ gav en hög räknehastighet i kammaren i förhållande till bakgrunden, och försvinnandet av $^{99}\text{Tc}^m$ från blodbanan var mycket långsamt. Den begränsade faktorn för upprepade bestämningar av ejektionsfraktionen var därför det fysikaliska sönderfallet för $^{99}\text{Tc}^m$. Denna märkningsmetod innebar även att radionuklid-angiokardiografi med lätthet kunde utföras med såväl första-passage- som jämviktstekniken.

2. Reproducerbarheten vid bestämning av RVEF med första-passagetekniken i vila var god, då metodfelet var lågt, 2.6 procentenheter.

Reproducerbarheten vid bestämning av LVEF med jämviktsteknik och en diastolisk kammarregion var god såväl i vila som under arbete. Metodfelet var 1.8 respektive 3.0 procentenheter.

3. I referensgruppen var LVEF med jämviktstekniken i vila $56\% \pm 8\%$. Under arbete ökade LVEF hos samtliga individer i referensgruppen.

I referensgruppen var RVEF i vila med första-passagetekniken $49\% \pm 5\%$. Under arbete var RVEF oförändrad eller ökade.

I referensgruppen var RVEF i vila med jämviktsteknik $43\% \pm 5\%$. Under arbete ökade RVEF.

4. Första-passagetekniken föreföll tillförlitligare än jämviktstekniken för bestämning av RVEF i vila och under arbete, eftersom metodfelet i vila var lägre, 2.6 mot 3.8 procentenheter, och då överensstämmelsen med hemodynamiska variabler var bättre.

5. RVEF syntas vara ett tillförlitligt mått på högerkammarfunktionen hos patienter med pulmonell hypertension, då RVEF mätt med första-passageteknik avslöjade högerkammardysfunktion lika bra som kateteriseringstekniken.
6. LVEF var ett bra mått på vänsterkammarfunktionen i vila och under arbete hos patienter med myokardinfarkt, koronarinsufficiens och pulmonell hypertension. LVEF avslöjade vänsterkammardysfunktion bättre än mätning av vänster kammares fyllnadstryck.

RIGHT AND LEFT VENTRICULAR EJECTION FRACTION AT REST AND DURING
EXERCISE ASSESSED WITH RADIONUCLIDE ANGIOCARDIOGRAPHY

Methodological aspects and comparison to simultaneously
obtained catheterization results in pulmonary
hypertension and in ischemic heart disease

Right (RVEF) and left ventricular ejection fraction (LVEF) assessed with radionuclide angiocardiology were compared to simultaneously obtained catheterization results at rest and during exercise in patients with pulmonary hypertension and ischemic heart disease. Methodological aspects of EF measurements were also investigated.

Blood pool imaging was performed with red blood cells (RBC) labelled with $^{99}\text{Tc}^{\text{m}}$ in vivo as this method gave more stable $^{99}\text{Tc}^{\text{m}}$ levels in blood compared to $^{99}\text{Tc}^{\text{m}}$ -labelled human serum albumin and because it was more convenient than labelling RBC in vitro. RVEF measured with first pass (FP) technique and equilibrium (EQ) technique correlated well at rest, $r = 0.86$, and during exercise, $r = 0.91$. The FP technique had the best reproducibility and reference values at rest were $49 \pm 5\%$ increasing with exercise. When $^{99}\text{Tc}^{\text{m}}$ and ^{133}Xe were compared to assess RVEF with FP technique, the correlation was good, $r = 0.88$. LVEF assessed with EQ technique and a fixed end-diastolic region of interest was very reproducible at rest and during exercise; reference values at rest were $56 \pm 8\%$ increasing with exercise.

In 10 patients with pulmonary hypertension significant negative correlations were found between RVEF assessed with FP technique and pressures in pulmonary artery and right atrium. Abnormal RVEF was found in all patients with right ventricular dysfunction. In 22 patients with recent myocardial infarction measurements of LVEF detected left ventricular dysfunction better than did measurement of pulmonary artery diastolic pressure. During effort angina in another 10 patients all had abnormal LVEF and abnormal hemodynamics. By combining ejection fraction and stroke volume, ventricular volumes were calculated at rest and during exercise.

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Cardiac Blood Pool Imaging – A Clinical Comparison between Red Blood Cells Labeled with ^{99m}Tc in vivo and in vitro and ^{99m}Tc -Labeled Human Serum Albumin

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In 25 patients undergoing radiocardiographic determination of ventricular function, three methods for blood pool imaging were compared. ^{99m}Tc was used to label human serum albumin (HSA) and red blood cells (RBC) *in vivo* or *in vitro*. The activity concentration of ^{99m}Tc in blood was measured during 2 hrs after injection and a significantly higher concentration was found with RBC compared to HSA already after 15 min. The left ventricular to background count rate ratio was significantly lower for HSA after 90 min compared to RBC. There was no statistical difference in ^{99m}Tc activity concentration in blood or in left ventricular to background count rate ratio during the two hrs when the two RBC-labeling procedures were compared. ^{99m}Tc -labeled RBC are superior to ^{99m}Tc -labeled HSA for gated blood pool studies and especially for repeated determinations of ventricular function. Because the *in vivo* labeling is the most convenient method it has been adopted as the clinical routine at our hospital.

Szintigraphie der kardialen Blutmasse – Ein klinischer Vergleich zwischen mit ^{99m}Tc in vivo und in vitro markierten Erythrozyten und ^{99m}Tc -Humanalbumin

Bei 25 Patienten, bei denen die Ventrikelfunktion radiokardiographisch untersucht wurde, wurden drei Methoden der Blutmassen-Szintigraphie verglichen. ^{99m}Tc wurde zur Markierung von Human-Serum-Albumin (HSA) und von Erythrozyten (RBC) in vivo oder in vitro verwendet. Die Aktivitätskonzentration des ^{99m}Tc im Blut wurde während 2 Std. nach der Injektion gemessen. Schon nach 15 Min. war die Konzentration des an die RBC gebundenen ^{99m}Tc signifikant größer als jene des an HSA gebundenen ^{99m}Tc . Die Quote der Impulsraten des linken Ventrikels und des Untergrundes war nach 90 Min. mit HSA signifikant kleiner als mit RBC. Es ergab sich keine statistische Differenz in der Aktivitätskonzentration des ^{99m}Tc im Blut oder in der Quote der Impulsraten des linken Ventrikels und des Untergrundes, wenn die beiden RBC-Methoden verglichen wurden. ^{99m}Tc -markierte Erythrozyten sind für die Blutmassen-Szintigraphie besser geeignet als ^{99m}Tc -markiertes HSA, besonders für wiederholte Bestimmungen der Ventrikelfunktion. Da die Methode mit in vivo markierten Erythrozyten die einfachste ist, wird sie als klinische Routinemethode in unserem Krankenhaus benützt.

The left ventricular ejection fraction (EF) and wall motion can be satisfactorily measured by electrocardiographically synchronized blood pool imaging, using radioactive tracers (1, 5, 9, 11). Repeated determinations can be done after a single radionuclide injection. The most commonly used agent at present is ^{99m}Tc -labeled human serum albumin (HSA) but because of its limited retention in the circulating blood, interest is now focused on red blood cells (RBC) labeled with ^{99m}Tc either in vivo (3, 8, 10) or in vitro (3, 6). However, most workers have so far only studied the retention for a very short time, mostly for less than one hour. The aim of the present investigation was to study the concentration of ^{99m}Tc in circulating blood during several hours after injection using in vitro and in vivo labeled RBCs as well as ^{99m}Tc -HSA in order to optimize late determination of EF and wall motion, e.g. during exercise or administration of drugs.

Material and Methods

25 consecutive patients with various heart diseases were studied. They were divided into three groups (see below) with no statistical difference according to age, height or weight.

Group A (7 subjects) was studied with ^{99m}Tc -HSA (Cardiolite[®], New England Nuclear), prepared in accordance with the manufacturers instructions.

Group B (9 subjects) was studied with in vivo labeled RBCs. A ^{99m}Tc -MDP kit, (Kabi Diagnostica, Nyköping, Sweden) routinely employed for skeletal scintigraphy and containing 5 mg sodium-methylendiphosphonate and 0.84 mg stannous chlorid, was used. It was dissolved in 4 ml saline and given intravenously 30 min before the injection of ^{99m}Tc -pertechnetate.

In group C (9 subjects) in vitro labeled RBCs were used. The labeling was carried out using the Brookhaven method with kits kindly provided by Dr. Richards (6).

In all subjects 300–370 MBq (8–10 mCi) ^{99m}Tc -pertechnetate were used. The ^{99m}Tc -pertechnetate was eluted from a column generator immediately before labeling so as to keep the content of ^{99m}Tc carrier as low as possible (4).

In order to reduce ^{99m}Tc uptake by the thyroid, all patients were given 200 mg sodium perchlorate immediately before injection of the radioactive tracer. Imaging of the heart was performed with a scintillation camera (Radicamera II) with the energy window at $140 \pm 15\%$ keV and a medium-resolution low-energy parallel-hole collimator. The left ventricular ejection fraction was determined with the camera in the left anterior oblique position with about 15° caudal tilt about 30 and 90 min after injection (2). The net left ventricular to background count-rate ratio was calculated, i.e. the count-rate over the left ventricle area minus the count-rate in the normalized surrounding background area divided by the latter. In order to determine the ^{99m}Tc activity concentration in blood,

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samples of blood were drawn at selected time intervals during 2 hrs. These concentration values were used to calculate the ^{99m}Tc activity concentration in blood normalized to the injected ^{99m}Tc activity per kg body weight. During the same period urinary excretion of ^{99m}Tc was determined.

The long-time retention of ^{99m}Tc-RBCs labeled in vivo and in vitro was studied in two patients up to 24 hrs after injection. Standard statistical methods (7) were used. A probability (P) of < 0.05 was considered significant.

Results

As may be seen from Fig. 1 the ^{99m}Tc concentration in whole blood showed a small decrease of about 6%/hr during the first 2 hrs after injection of in vitro labeled RBCs.

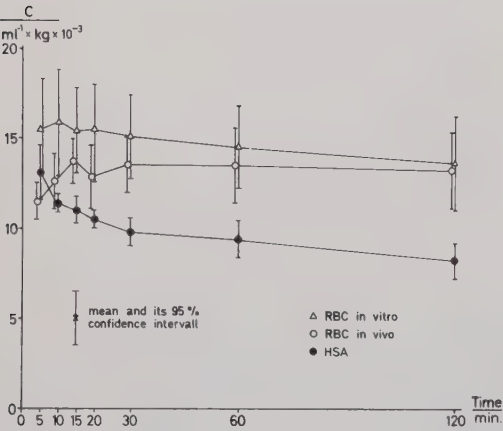


Fig. 1: ^{99m}Tc activity concentration (MBq · ml⁻¹) in whole blood drawn at various times after injection divided by injected ^{99m}Tc activity per kg body weight (MBq · kg⁻¹). Data are given for three different compounds, RBCs labeled in vitro and in vivo as well as HSA. The results have been corrected for physical decay of ^{99m}Tc.

With in vivo labeled RBCs the ^{99m}Tc concentration in blood increased during the first 10–15 min after injection and then remained at a level not significantly different from that of in vitro labeled RBCs. In the albumin group the ^{99m}Tc concentration in blood was

after 15 min significantly lower than that in the other two groups. During the first 30 min the decrease was more rapid than subsequently.

The net left ventricular to background count-rate ratios after 30 and 90 min are shown in Table I for the various preparations. The urinary excretion of ^{99m}Tc during the first 2 hrs after injection is also given in Table I.

Discussion

The in vivo and in vitro labeled RBCs gave essentially the same activity concentration in blood 10 min after the ^{99m}Tc injection. During the first 10–15 min after injection there was however a considerable increase in activity concentration in blood when in vivo labeling was used. The explanation might be that ^{99m}Tc-per-technetate which initially had left the vascular space, gradually returned to the blood pool, and labeled RBCs during the first 10 min.

^{99m}Tc-HSA showed a significantly lower activity concentration in blood after 10–15 min compared to both RBC methods. This was most likely due to the leakage of albumin from the vascular space.

With all three methods the net count-rate ratio between left ventricle and background was about the same after 30 min. After 90 min the ratio was significantly lower for HSA which is in accordance with the blood activity concentration. A ratio of about 1 or higher makes it more easy to delineate the left ventricle and thus determine wall motion and ejection fraction. However, in one patient studied with HSA the ratio after 90 min was zero and the left ventricle could not be seen at all. Figs. 1 and 2 show that the retention in circulating blood of ^{99m}Tc-RBCs labeled either in vivo or in vitro is good. These results are in agreement with those of Thrall et al. (10) and Hegge et al. (3). Thus with RBC labeling the limiting factor for repeated blood pool studies after a single injection is the physical decay of ^{99m}Tc.

Table I: Net left ventricular to background count-rate and urinary excretion of ^{99m}Tc.

	End-diastolic count-rate – background count-rate background count-rate		Percent of injected ^{99m} Tc in urine during the 2 hrs after injection (Mean ± SE)
	After 30 min (Mean ± SE)	After 90 min (Mean ± SE)	
Group A	0.93 ± 0.06 (n=7)	0.58 ± 0.15 (n=5)	9.1 ± 1.8 (n=5)
Group B	1.02 ± 0.08 (n=9)	0.99 ± 0.11 (n=6)	4.6 ± 0.6 (n=5)
Group C	1.06 ± 0.13 (n=7)	1.17 ± 0.22 (n=4)	5.4 ± 1.1 (n=7)

Group A = ^{99m}Tc-HSA
Group B = ^{99m}Tc RBCs labeled in vivo
Group C = ^{99m}Tc RBCs labeled in vitro

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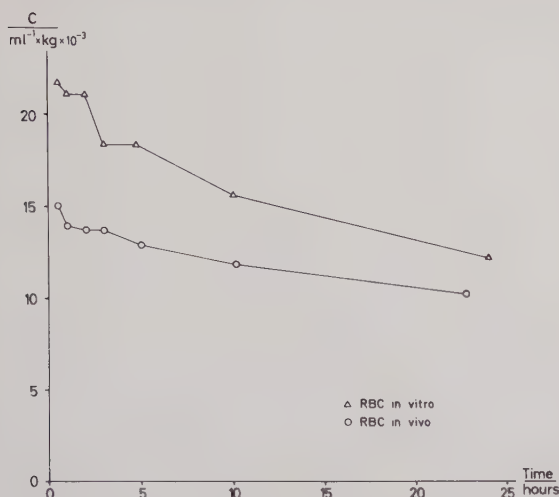
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Fig. 2: ^{99m}Tc activity concentration ($\text{MBq} \cdot \text{ml}^{-1}$) in whole blood drawn at various times after injection divided by injected ^{99m}Tc activity per kg body weight ($\text{MBq} \cdot \text{kg}^{-1}$).

Data are given for two patients, one with RBCs labeled in vitro, the other with RBCs labeled in vivo. The results have been corrected for physical decay of ^{99m}Tc .

The urinary excretion of ^{99m}Tc is slightly higher when albumin is used rather than RBCs. This would possibly indicate that the albumin labeling is slightly less stable.

Conclusion

Both the in vitro and in vivo labeled RBCs are superior to albumin for repeated equilibrium blood pool scintigraphy and ejection fraction determinations. Because the in vivo labeling is the most convenient method it has been adopted as the clinical routine method for blood pool studies in our hospital.

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RADIONUCLIDE ASSESSMENT OF RIGHT VENTRICULAR
EJECTION FRACTION
A comparison of first pass studies
with ^{133}Xe and $^{99}\text{Tc}^m$

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SUMMARY

Right ventricular ejection fraction (RVEF) was determined in 26 patients using the first pass radionuclide angiocardiography with ^{133}Xe and $^{99}\text{Tc}^m$ as tracers. A good correlation ($r = 0.88$) was found. Duplicate determinations in 13 patients with ^{133}Xe showed good reproducibility, the absolute value for the standard error of a single determination being 2.6% and the coefficient of variation 5.7%. In 17 healthy individuals RVEF was $49 \pm 5\%$ (range 42-61%). It is concluded that ^{133}Xe can be used for RVEF determinations. Due to the rapid elimination and the low radiation dose ^{133}Xe is preferable when repeated determinations of RVEF are desired.

INTRODUCTION

The ejection fraction is a well accepted clinical index of ventricular function (Cohn & Gorlin 1975; Sonnenblick & Strobeck 1977). Most often the functional evaluation concerns the left ventricle, but an increased attention has been drawn to the right ventricle (Cohn & Gorlin 1975; Pitt 1976; Nichols 1980). Right ventricular ejection fraction (RVEF) can be assessed with ventriculography (Ferlinz 1976) or radionuclide angiography (Steele et al. 1976; Berger et al. 1978; Tobinick et al. 1978). The radionuclide method has the advantage that no assumption of the geometry of the right ventricle is required.

In order to assess the functional reserve of the ventricles, ejection fractions have been measured during exercise (Borer et al. 1977). For the left ventricular ejection fraction (LVEF) this can be performed with the first pass or the equilibrium radionuclide angiocardiology (Borer et al. 1977; Rerych et al. 1978). For RVEF assessment the equilibrium technique has been described (Maddahi et al. 1979; Slutsky et al. 1980), but this technique presents problems because of superimposition of the right atrial activity into the right ventricle (Maddahi et al. 1979; Slutsky et al. 1980; Weens & Gay, Jr. 1970). Thus, RVEF most often is determined during the first passage of the tracer through the right ventricle. Thus, measurement of the changes from rest to exercise necessitates two injections. This gives a higher radiation dose to the patient and the background level will differ between the two investigations. There is a need of a tracer with short half-life for such studies. In this study ^{133}Xe , a tracer with short biological half-life, is compared with $^{99}\text{Tc}^m$ in the determination of RVEF with first pass radionuclide angiocardiology.

MATERIAL AND METHODS

Material

In 26 patients with various cardiac and pulmonary diseases referred to the Department of Clinical Physiology for radionuclide angiography and assessment of LVEF, we determined RVEF using the tracers ^{133}Xe and $^{99}\text{Tc}^m$. In 13 of these patients we performed duplicate determinations of RVEF with ^{133}Xe .

Reference values for RVEF were obtained from four healthy volunteers and 13 patients aged 40 ± 10 (mean $\pm$ SD). These 13 patients were referred to the laboratory for measurements of ejection fraction on the suspicion of left ventricular dysfunction. RVEF in these individuals were assessed with $^{99}\text{Tc}^{\text{m}}$ -pertechnetate using the first pass technique. At the final clinical evaluation of these subjects, however, it was concluded that there was no proof of cardiac dysfunction. Informed consent was obtained from each patient.

Procedure

The patients were investigated in the supine position. A polyethylene catheter (PE 160) was percutaneously inserted through an antecubital vein and passed to the superior caval vein. The gamma-camera projection was right anterior oblique (RAO) 30° . In this projection it is easy to separate the right ventricle from the right atrium and the pulmonary artery (Weens & Gay, Jr. 1970). The radionuclide was placed in an extension (volume 3 ml) of the catheter, which then was rapidly flushed with 20 ml saline. The activity of the ^{133}Xe -solution was about 750 MBq (20 mCi) and the volume never exceeded 3 ml. The $^{99}\text{Tc}^{\text{m}}$ activity was 350 MBq (9.5 mCi) in less than 1 ml. Since it was not possible to achieve a higher ^{133}Xe concentration, different tracer volumes were used. The patients rested for 15 minutes before the first injection which always contained ^{133}Xe . When most of the xenon had been washed out after about five minutes, the $^{99}\text{Tc}^{\text{m}}$ -pertechnetate injection or the second ^{133}Xe injection was performed. In most patients the radionuclide angiography with $^{99}\text{Tc}^{\text{m}}$ also included an equilibrium study of the left ventricle with in vivo red blood cell labelling (Dahlström et al. 1979).

The mean whole body radiation dose for one injection of ^{133}Xe was estimated to be 0.2 mGy (Atkins et al. 1980; Johansson, Mattsson & Nosslin 1981). For $^{99}\text{Tc}^{\text{m}}$ the mean whole body radiation dose was 1.6 mGy if in vivo red blood cell labelling was performed, otherwise 1.3 mGy (Johansson, Mattsson & Nosslin 1981). The latter procedure gives the highest local, absorbed doses, i.e. to gastro-intestinal organs.

Equipment

The gamma-camera was a Radicamera II with a general purpose parallel-hole collimator. Energy windows for ^{133}Xe and $^{99\text{Tc}m}$ were set at $81 \text{ keV} \pm 15\%$ and $140 \text{ keV} \pm 15\%$, respectively. The data handling was performed using NUKAB 2530-system. The dynamic gamma-camera data were collected in list mode together with an R-wave signal from the ECG. The maximum permissible count rate in list mode was $43,000 \text{ s}^{-1}$, whereas the maximum count rate during these studies was about $30,000 \text{ s}^{-1}$. The losses due to dead time never exceeded 5% and were not corrected for.

Data reconstruction

The first passage study was reconstructed in 40 ms frames and a preliminary region of interest (ROI) for the right ventricle was chosen. From the time activity curve in this ROI diastolic and systolic time intervals were selected from which pictures were generated. These pictures were used to better define the valve planes displaying them as a movie and subtracting them to get a stroke volume picture. A final diastolic ROI for the right ventricle was then manually outlined from the diastolic picture. A background ROI was automatically placed two matrix elements wide and two matrix elements outside the ventricle without overlapping cardiac or great vessel structures. During the right ventricular passage one mean R-R-interval (Folland et al. 1977) formed by two to four beats was reconstructed in sequential 40 ms frames starting 200 ms before the R-wave. These beats were chosen from the downslope of the preliminary right ventricular time activity curve. After subtraction of the normalized background count rate ejection fraction was calculated as:

$$\frac{\text{end-diastolic count rate} - \text{end-systolic count rate}}{\text{end-diastolic count rate}}$$

from the time activity curve generated from this mean R-R-interval.

Statistics

Standard statistical equations were used. The standard error of a single determination (e) was obtained from duplicate measurements according to Dahlberg (1940) using the formula:

$$e = \sqrt{\frac{\sum d^2}{2n}}$$

where n is the number of duplicate measurements and $\sum d^2$ is the sum of the squares of the differences.

RESULTS

Fig. 1 shows a typical time activity curve during the first passage through the right ventricle. By synchronously adding two to four beats an R-wave synchronized composite curve is received (Fig. 2) from which RVEF is calculated. RVEF determined in this way using first ^{133}Xe and then $^{99}\text{Tc}^{\text{m}}$ as the radioactive tracers in 26 patients showed a good correlation, $r = 0.88$ (Fig. 3). The heart rate did not differ during the two injections and was 70 ± 17 and 70 ± 15 (mean $\pm$ SD) beats per minute, respectively. Fig. 4 shows time activity curves from the right ventricle, normalized to 100% at end-diastole, during the mean R-R interval in a patient investigated with ^{133}Xe and $^{99}\text{Tc}^{\text{m}}$. Duplicate measurements of RVEF with ^{133}Xe in 13 patients also showed a good correlation, $r = 0.90$ (Fig. 5), and the absolute value for the standard error of a single determination was 2.6%. As the mean of these 13 duplicate measurements was 45.2%, the coefficient of variation was 5.7%. The heart rate during the first and second xenon-injection did not differ significantly and was 64 ± 16 and 65 ± 16 beats per minute, respectively. In 17 healthy individuals RVEF was $49 \pm 5\%$ and the range 42 - 61%. Their heart rates were 68 ± 11 beats per minute.

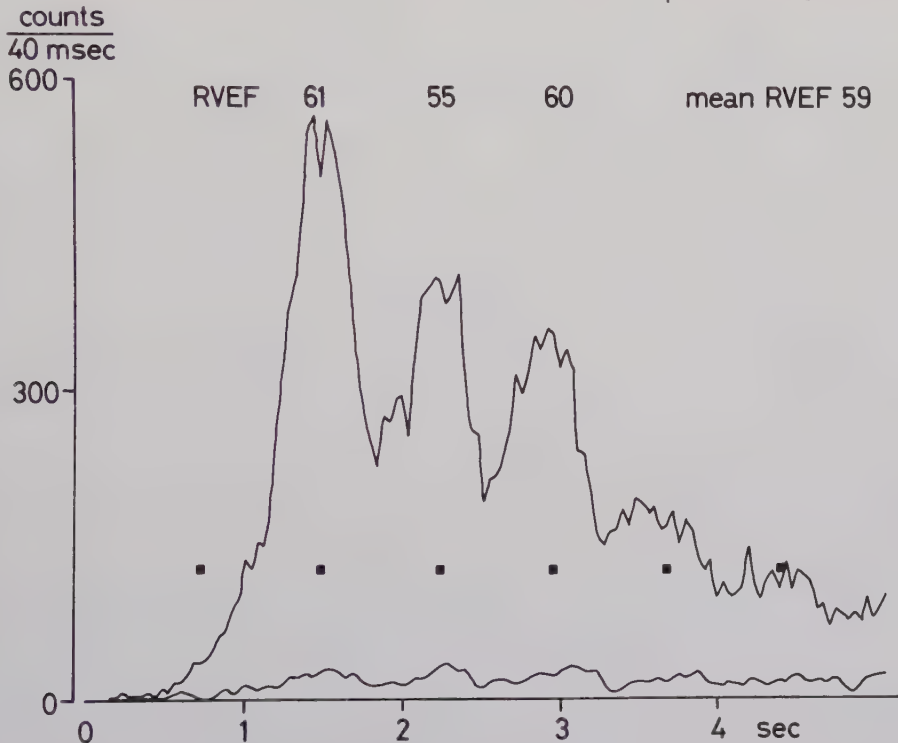


Fig. 1. Typical right ventricular and background time activity curve during the first passage. ■ representing the R-wave in ECG. RVEF = right ventricular ejection fraction in per cent.

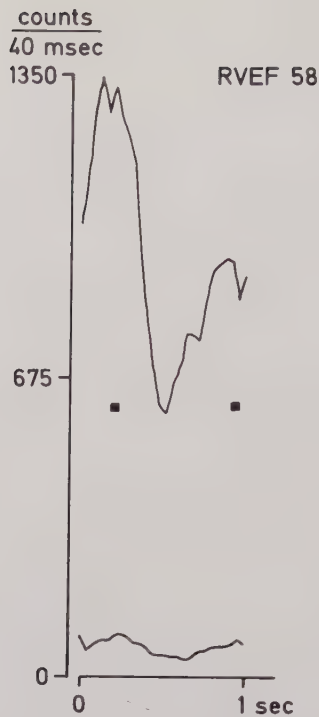


Fig. 2. Time activity curve for the right ventricle and background during the mean R-R-interval reconstructed from the second, third and fourth R-R-interval during the first passage in Fig. 1. Symbols as in Fig. 1.

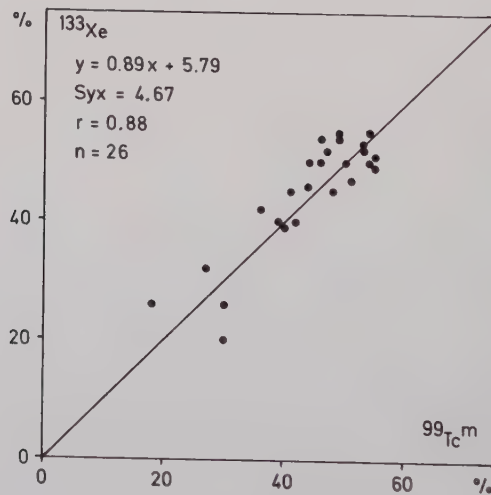


Fig. 3. Comparison of the right ventricular ejection fraction (in per cent) assessed with ^{133}Xe and $^{99}\text{Tc}^{\text{m}}$ during the first passage in 26 patients. S_{yx} = residual standard deviation. The line of identity is given.

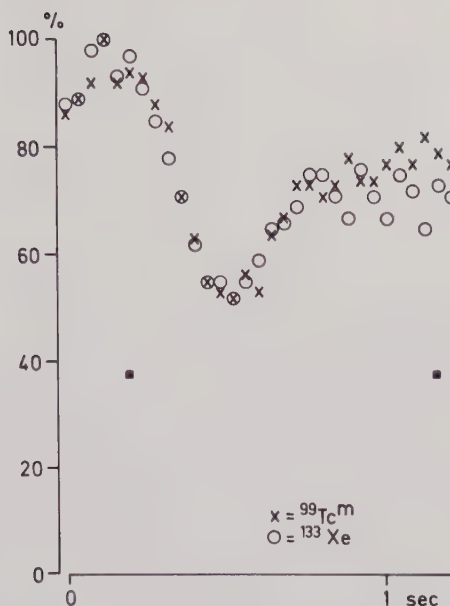


Fig. 4. Right ventricular time activity curve during the mean R-R-interval assessed with ${}^{133}\text{Xe}$ and ${}^{99}\text{Tc}^m$ in one patient. The end-diastolic count rate in both studies has been normalized to 100%. ■ representing the R-wave in ECG.

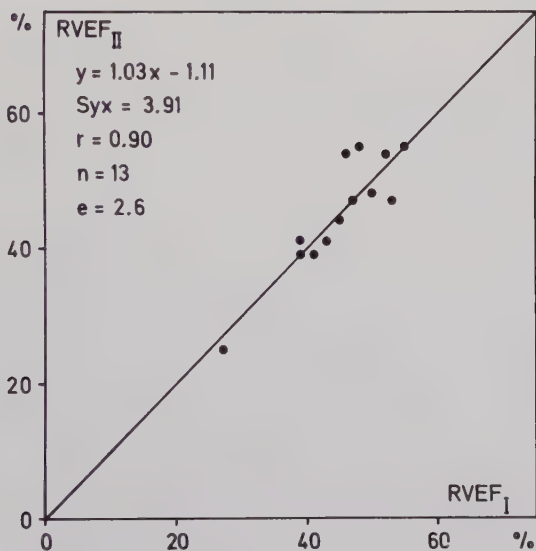


Fig. 5. Duplicate determinations of right ventricular ejection fraction (RVEF) with ${}^{133}\text{Xe}$ during the first passage in 13 patients. S_{yx} = residual standard deviation. The line of identity is given. The standard error of a single determination (e) is calculated using the formula:

$$e = \sqrt{\frac{\sum (RVEF_I - RVEF_{II})^2}{2n}}$$

DISCUSSION

It is difficult to obtain a projection of the right ventricle free from other cardiac structures in the left anterior oblique (LAO) projection due to the anatomy of the heart. This is because of a higher degree of overlapping of the atrium and ventricle on the right side than the left side (Takahashi 1969; Weens & Gay, Jr. 1970; Pernkopf 1980). Nevertheless, the LAO-projection has been described for RVEF assessment using the equilibrium radionuclide method (Maddahi et al. 1979; Slutsky et al. 1980). However, most authors have used the first pass technique with the gamma-camera in RAO projection for RVEF assessment (Steele et al. 1976; Tobinick et al. 1978) or the anterior projection when using smaller multicrystal scintillation cameras (Berger et al. 1978). Especially in RAO projection there is no or minimal overlapping of the right atrium and the right ventricle. Even in this projection, however, there may be some difficulties in outlining the right ventricle in patients with a dilated right atrium. In these patients the stroke volume picture is valuable. During the first passage through the right heart there is no activity in the left heart.

Thus, the RAO projection should be preferred in first pass studies of the right ventricle. Using this projection Steele et al. (1976) have reported a good correlation between RVEF assessed with ventriculography and first pass radionuclide angiography. There are some disadvantages with first pass studies. One is the limited time to collect data which will impede the amount of counts to be collected. Thus, these studies will suffer somewhat from statistical limitations (Holman & Parker 1981).

Another disadvantage is related to the mixing in the right ventricle (Maseri & Enson 1968). When the bolus enters the right ventricle a comparatively large fraction of the activity will be ejected with the first beat. Subsequently the activity is distributed to the apex. Blood with less activity then enters the ventricle and is to a large fraction ejected together with a smaller fraction of activity from the apex, and so on. Thus, ejection fraction calculated from the first transit curve may be high at the first beat and more correct at the mid-portion of the curve and low at the end of the bolus passage. These mixing problems seem to be larger in normal subjects than in patients with low stroke volume. In the present study only beats (usually two-four) on the downslope of

the time activity curves were chosen for the averaging process. Even if the mixing problem cannot be fully avoided, the reproducibility of the measurement of RVEF was quite good, the coefficient of variation in duplicate measurements being 5.7%. For repeated measurements of RVEF with this first pass method a tracer with rapid disappearance is desirable in order to minimize problems with background.

As ^{133}Xe is used for regional lung function studies at our laboratory it was convenient for us to test it for radionuclide angiography. Other suitable radionuclides are ^{81}Kr and ^{127}Xe . ^{81}Kr which has a very short half-life, 13 seconds, is not possible to use everywhere since the ^{81}Kr -generator also has a very short half-life. For ^{127}Xe -studies a medium energy collimator with its poorer resolution is needed. Thus, ^{127}Xe is not a more favourable tracer than ^{133}Xe . On the other hand, ^{133}Xe is not an ideal radionuclide for gamma-camera studies since its energy is low, 81 keV. At this low energy the inherent resolution of the gamma-camera is worse and the tissue attenuation is higher than at 140 keV. The low radiation dose which ^{133}Xe gives to the patient is of course attractive. When using ^{133}Xe the mean whole body radiation dose is about 1/6 of that of $^{99}\text{Tc}^{\text{m}}$ -pertechnetate and corresponds to one minute of fluoroscopy (M. Gustavsson: Personal communication). This is due to the rapid tracer elimination from the body during the respiratory wash-out. This rapid disappearance of ^{133}Xe also implies almost the same background activity in serial determinations. A correction of the right ventricular time activity curve for background activity (Figs. 1 and 2) does not affect RVEF very much (about 5%). Little activity has reached the lung when the count rate is highest in the right ventricle, so RVEF can be assessed without background correction. For serial determinations with varying background activities, correction is of course necessary.

The 81 keV-photon production per disintegration is low for ^{133}Xe but this can partly be compensated for by increasing the activity given. Thus, the count rate during the first passage usually was about 25% less during ^{133}Xe -passage than during $^{99}\text{Tc}^{\text{m}}$ -pass with the activities used. Nevertheless, the correlation between the RVEF determined with the two tracers is good, as can be seen in Fig. 3. The variation coefficient of 5.7% for duplicate measurements is slightly higher than for LVEF assessed with the equilibrium method (Dahlström et al. unpublished work) but of the same magnitude as is reported for cardiac output (Malmcrona 1964). The higher volume of the ^{133}Xe -bolus, less than 3 ml,

followed by 20 ml saline, compared to the $^{99}\text{Tc}^{\text{m}}$ -bolus, less than 1 ml followed by 20 ml saline, did not seem to affect the comparison as no systematic difference could be detected. As shown in the figures the distribution around the lines of identity is about the same when duplicate ^{133}Xe -determinations (Fig. 5) or ^{133}Xe - $^{99}\text{Tc}^{\text{m}}$ determinations (Fig. 3) were compared.

The reference values for RVEF found in this study are slightly lower than those reported by Tobinick et al. (1978) and Berger et al. (1978). They found normal RVEF to be 52% and 55%, respectively, with about the same dispersion around the mean as in this study. Berger et al. (1978) used a multicrystal scintillation camera in anterior projection. The overlapping of the right atrium and the right ventricle is compensated for by background subtraction. This background region is placed over the right atrium. Thus, the higher background subtraction in their study may explain the somewhat higher RVEF in their healthy subjects.

Tobinick et al. (1978) used the same camera projection and the same background subtraction method as in this study. The only difference is that they calculated RVEF beat by beat from top to valley for several beats and then used the mean as RVEF. However, the R-wave synchronized composite technique used in this study, adds activity synchronously starting from the R-wave. Thus, the tops and valleys can be somewhat smoothed. This can explain the slightly lower RVEF in normal subjects found in our study. The advantage of the R-wave synchronized composite technique is the higher count rate and thus less statistical uncertainty. The disadvantage is that the technique needs regular cardiac rhythm. Using the equilibrium method Maddahi et al. (1979) and Slutsky et al. (1980) reported normal RVEF to be about $48\% \pm 5\%$ and $49\% \pm 10\%$, respectively. Tobinick et al. (1978) also reported an average variation of 3.4% in six patients with normal RVEF given 300 MBq (8 mCi) $^{99}\text{Tc}^{\text{m}}$ -DTPA (diethylene triamine penta acetate) within 30 minutes. In their comparison of course the background activity varied between the first and the second determination. Thus, the small difference in variation compared with this study is not necessarily due to different reproducibility. The conclusion of this study is that RVEF assessed with ^{133}Xe is as accurate as RVEF assessed with $^{99}\text{Tc}^{\text{m}}$. As the error of a single determination for RVEF is small and the radiation dose low, the Xe-method is suitable for serial determinations of RVEF during exercise or after the administration of drugs.

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SIMULTANEOUS ASSESSMENT OF RIGHT VENTRICULAR
EJECTION FRACTION AND CENTRAL HEMODYNAMICS AT
REST AND DURING EXERCISE IN PATIENTS WITH
PULMONARY HYPERTENSION

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SUMMARY

In ten patients, aged 55-73, with pulmonary hypertension right ventricular ejection fraction (RVEF) was measured simultaneously with central hemodynamics twice at rest and during exercise. In the first investigation RVEF was measured with first pass (FP) radionuclide angiocardiology using ^{133}Xe and $^{99}\text{Tc}^m$ as tracers. In the second investigation after one hour's rest RVEF was measured with equilibrium (EQ) radionuclide angiocardiology. Significant correlations were found between RVEF and pulmonary artery pressure ($r = -0.74$ to -0.88) and between RVEF and right atrial pressure ($r = -0.76$ to -0.84) at rest and during exercise. RVEF was low or decreased during exercise in all patients with hemodynamic signs of right ventricular failure. Good correlations were found between the FP and EQ techniques for measuring RVEF both at rest, $r = 0.86$, and during exercise, $r = 0.91$. RVEF measured with the FP technique showed better reproducibility, better correlation to hemodynamic variables and to history of right ventricular failure. LVEF at rest or during exercise was abnormal in six patients. There was no correlation between RVEF and LVEF.

INTRODUCTION

The survival of patients with chronic pulmonary disease (CPD) has been linked to the presence and degree of pulmonary hypertension (PH) (Burrows et al., 1972; Ourednik & Susa, 1975; Weitzenblum et al., 1979).

The clinical diagnosis of early PH is difficult. Clinical signs may fail until overt right ventricular failure exists (Piemme, 1972). For a definite diagnosis and to quantify PH, invasive measurements of pulmonary artery pressure are often needed.

Detection of PH with noninvasive methods is also difficult. ECG and chest X-ray will fail to detect about 50% of the patients with PH (Matthys et al., 1972a, b). Even in PH with right ventricular failure these methods will be negative in about 30% of the cases (Matthys, 1974; Widimský, 1978).

Thus, better noninvasive methods are needed for the diagnosis and the follow-up of patients with PH and right ventricular dysfunction.

Radionuclide angiocardigraphy has been used to measure right (RVEF) and left (LVEF) ventricular ejection fractions (Steele et al., 1976; Ashburn, Schelbert & Verba, 1978). Radionuclide angiocardigraphy can be performed in two ways, the first pass (FP) (Steele et al., 1976; Ashburn, Schelbert & Verba, 1978) and the equilibrium (EQ) radionuclide angiocardigraphy (Ashburn, Schelbert & Verba, 1978; Maddahi et al., 1979; Slutsky et al., 1980b).

In the present study patients with PH were investigated with the following purposes: Firstly, to compare RVEF to the simultaneously measured catheterization variables at rest and during exercise in the evaluation of PH and right ventricular function; secondly, to compare the first pass and the equilibrium technique in the measurement of RVEF at rest and during exercise. In addition, the relation between RVEF and clinical or lung function variables was also studied as was the occurrence of left ventricular dysfunction in PH.

MATERIAL AND METHODS

Patients

The patients studied were six men and four women, with a mean age of 65 years (range 55-73) referred to the Department of Clinical Physiology for hemodynamic evaluation due to CPD. Their clinical characteristics and pulmonary function data are presented in Table 1. No patient had clinical signs of coronary artery disease or valvular heart disease and all were in sinus rhythm. Two patients (AS and PG) were treated for systemic arterial hypertension. Informed consent was obtained from each patient.

Catheterization technique

A heart catheter was percutaneously inserted into a cubital vein and passed to the pulmonary artery. A thin polyethylen catheter (PE 160) was inserted into the brachial artery and another one was inserted into a cubital vein and passed to the superior caval vein and the right atrium.

Right atrial (RA), pulmonary artery (PA), pulmonary capillary venous (PCV) and brachial artery (BA) pressures were recorded with conventional equipment (pressure transducer 746 and Mingograph 81 from Siemens-Elema AB, Stockholm, Sweden). The supine zero level was taken 5 cm behind the sternum angle. Mean pressures were obtained by electrical damping. Cardiac output was measured by the dye dilution technique (bromsulphalein) (Wassén, 1956). Pulmonary vascular resistance was calculated as the difference between PA mean and PCV mean pressure divided by the cardiac index. Blood gas analyses were performed with conventional equipment (Instrumentation Laboratories Inc., Boston, U.S.A.).

Spirometry

Routine spirometry was performed with a Bernstein-type spirometer and included measurements of vital capacity (VC) and forced expiratory volume in one second (FEV_{1.0}) in sitting position. Predicted values were taken from the reference material of this laboratory.

Table 1

Clinical and pulmonary function data in the patients studied

M = male; F = female; Medical treatment: a = digitalis; b = diuretic; c = cortisone; d = bronchodilator; RVF = history of right ventricular failure; ECG = electrocardiographic signs of: P = P-pulmonale; RBBB = right bundle branch block; RV = right ventricular hypertrophy; LV = left ventricular hypertrophy; HV = heart volume; VC = vital capacity; FEV_{1.0} = forced expiratory volume in one second; aB-PaO₂ = arterial oxygen tension; aB-PCO₂ = arterial carbon dioxide tension; HCT = hematocrit.

Patient	Age/Sex years	Medical treatment	RVF	ECG	HV ml · m ⁻²	VC % pred.	FEV _{1.0} l BTPS/% pred.	aB-PaO ₂ kPa	aB-PCO ₂ kPa	HCT %	Diagnosis
ES	68 M	abc	+	P	570	63	0.87/31	6.4	8.3	52	Chronic bronchitis.
EJ	60 F	abc	+	P	470	71	0.60/30	8.1	5.5	48	Pulmonary emphysema.
YJ	64 M	abcd	+	RBBB	880	75	1.47/50	5.9	7.8	66	Chronic bronchitis. Bronchial asthma.
SM	61 F	cd	+		440	83	1.95/76	11.9	4.3	41	Bronchial asthma.
IL	71 F	ab	+	P; RV	450	69	1.52/67	8.4	4.5	58	Primary pulmonary hypertension.
AS	66 F	ab		P; LV	345	52	1.22/49	6.8	6.3	46	Pulmonary fibrosis. Arterial hypertension.
PG	59 M	-			575	62	2.66/79	10.5	5.4	44	Asbestosis. Arterial hypertension.
EK	73 M	abd			475	69	0.92/28	6.7	6.7	47	Chronic bronchitis.
EP	55 M	cd			535	91	1.87/49	12.5	3.9	43	Bronchial asthma.
GN	72 M	bcd			420	58	0.87/25	10.5	4.2	30	Chronic bronchitis. Bronchial asthma. Sideropenic anemia.
Mean	65				516	69	1.40/48	8.8	5.7	48	
S.D.	6				146	12	0.63/20	2.4	1.5	10	

Radionuclide angiocardiology

RVEF and LVEF were measured at rest and during exercise using the FP and the EQ radionuclide angiocardiology. A gammacamera (Radicamera II) with a low energy all purpose parallel-hole collimator was used. The data handling was performed by means of a NUKAB 2530 system. The registrations were recorded in list mode simultaneously with an R-wave marker from the electrocardiogram. The maximum permissible count rate in list mode was $43,000 \text{ s}^{-1}$. The losses due to dead time never exceeded 5% and were not corrected for.

(A) First pass radionuclide angiocardiology: The gammacamera projection was 30° right anterior oblique. At rest only RVEF was measured. The tracer ^{133}Xe , 740 MBq (20 mCi) in a volume less than 3 ml, was placed in an extension of the superior caval vein catheter which then was rapidly flushed with 20 ml saline. ^{133}Xe was used at rest with the intention of minimizing the background activity for the next FP study during exercise, when 350 MBq (9.5 mCi) $^{99}\text{Tc}^m$ was injected with the same camera projection. The registered data were reconstructed in 40 ms frames and fixed end-diastolic regions of interest for the right and left ventricles were defined. The background regions of interest were taken two matrix elements wide and two matrix elements outside the corresponding ventricular regions and were not allowed to overlap cardiac structures or great vessels (Dahlström, in press).

Time activity curves were generated and after background subtraction, ejection fraction was calculated as (end-diastolic count rate - end-systolic count rate)/end-diastolic count rate.

Good agreement has previously been found when RVEF was measured with ^{133}Xe and $^{99}\text{Tc}^m$ as tracers (Dahlström, in press).

(B) Equilibrium radionuclide angiocardiology: Blood pool imaging was performed with in vivo red blood cell labelling with 500 MBq (13.5 mCi) $^{99}\text{Tc}^m$ (Dahlström et al., 1979). Thus, besides the $^{99}\text{Tc}^m$ -dose given during the exercise FP study another 150 MBq (4 mCi) was injected immediately after exercise, a higher activity than 350 MBq $^{99}\text{Tc}^m$ given as a bolus might exceed the maximum permissible count rate of the gammacamera-computer system.

The camera projection was a modified left anterior oblique (LAO) view with a caudal tilt of about 15°. The angle that optimally separated the ventricles was chosen (about LAO 30°).

The collection time for the EQ study at rest and during exercise was about 2 minutes. This registration was started when the patients had rested for 60 minutes after the first exercise test.

Data reconstruction and the definition of a fixed end-diastolic left ventricular and background regions of interest will be reported elsewhere (Dahlström, Ohlsson & Lilja, in press).

RVEF was calculated according to the technique described by Maddahi et al. (1979).

Radiation dose

The mean whole body radiation dose due to the ^{133}Xe and $^{99\text{Tc}}\text{m}$ doses were calculated to be 0.2 mGy (20 mrad) and 2.3 mGy (230 mrad), respectively (Johansson, Mattsson & Nosslin, 1981).

Procedure

After insertion of the catheters the patients rested for at least 20 minutes. Measurements of central hemodynamics and ejection fractions were performed twice at rest and during exercise. This was done to allow a comparison between the FP and the EQ technique in measuring RVEF at rest and during exercise. After the first measurements at rest and during exercise, the patients rested for one hour. The dye injection for cardiac output measurements was immediately followed by the radionuclide bolus injection, when the FP radionuclide angiocardiology was used, i.e. during the first investigation. During the second investigation cardiac output was measured in the middle of the collection time for the EQ radionuclide angiocardiology. Pressures were measured during at least five respiratory cycles before and after the cardiac output measurement and the mean values are given. The exercise test was performed in supine position on the catheterization table with the pedals elevated 44 cm above the table level.

Statistical methods

Standard statistical equations were used. Data are expressed as the mean $\pm$ standard deviation. Differences were calculated with Student's t-test. A probability (P) value of < 0.05 was considered significant. The standard error of a single determination (e) was calculated from duplicate registrations according to Dahlberg (1940) using the formula:

$$e = \sqrt{\frac{\sum d^2}{2n}}$$

where n is the number of duplicate measurements and $\sum d^2$ is the sum of the squares of the differences.

Reference values

Reference values for catheterization variables were obtained from Malmberg (1965) with correction for different zero levels. Using the EQ radionuclide angiocardiology in 12 healthy subjects with a mean age of 36 years, range 18-51, reference values for LVEF and RVEF were found to be $56 \pm 8\%$ and $43 \pm 5\%$, respectively, at rest and $61 \pm 8\%$ and $49 \pm 6\%$, respectively, during mild supine exercise (50 W) (Dahlström, unpublished data). Reference values for RVEF at rest and during exercise using the FP radionuclide angiocardiology were $49 \pm 5\%$ (n = 17) (Dahlström, in press) and $53 \pm 2\%$ (n = 5) (Dahlström, unpublished data). None of the healthy subjects decreased their RVEF during exercise.

Previous reports in healthy subjects have also shown that RVEF increased during exercise except in a few cases where RVEF did not change (Berger et al., 1979; Johnson et al., 1979; Slutsky et al., 1980b). Thus, a decrease in RVEF during exercise was considered abnormal.

RESULTS

(A) Catheterization results

At rest all but two patients had PH and all patients had PH during exercise, the PA mean pressure increased from 27 ± 17 mm Hg at rest to 51 ± 19 mm Hg during exercise. The mean work load was 27 ± 12 watt. The individual catheterization results are presented in Table 2. All except one patient (SM) had high pulmonary vascular resistance at rest and during exercise. At rest one patient had a high RA mean pressure and during exercise five more had so. At rest no patient had a high PCV mean pressure, while three patients had pathologically high PCV mean pressures during exercise.

When the two investigations, performed with one hour's interval, were compared, no statistically significant difference was found in RA, PA or PCV mean pressure at rest or during exercise (Table 2). Neither were there any significant differences in cardiac index, BA mean pressure or pulmonary vascular resistance. Stroke index, however, was slightly but significantly lower at the second investigation at rest and during exercise. The fall was 2.5 ± 2.6 ml $\cdot$ m⁻² ($p < 0.05$) and 4.4 ± 3.1 ml $\cdot$ m⁻² ($p < 0.01$), respectively. At rest no significant difference between the two measurements was found in heart rate. During exercise, however, heart rate increased 3 ± 4 beats $\cdot$ min⁻¹ ($p < 0.05$) at the second measurement (Table 2).

(B) Right ventricular ejection fraction

There was no significant difference between RVEF measured with the FP and the EQ technique at rest or during exercise and the correlation between the techniques was good, $r = 0.86$ at rest, $r = 0.91$ during exercise and $r = 0.88$ when the observations at rest and during exercise were pooled (Fig. 1). The individual values of ejection fraction are given in Table 3. At rest two patients had a low RVEF measured with the two techniques. During exercise RVEF was low or decreased in four more patients when measured with the FP technique. When measured with the EQ technique, RVEF was low or decreased in three more patients compared to rest.

Table 2

Catheterization results at rest and during exercise in the patients studied
(I = first investigation; II = second investigation)

Reference values $\bar{X} \pm 2$ SD	MEAN PRESSURES (mm Hg)				HEART RATE (beats $\cdot$ min ⁻¹)				STROKE INDEX (ml $\cdot$ m ⁻²)	
	Right atrium		Pulmonary artery		Pulmonary capillary venous					
	rest	exercise	rest	exercise	rest	exercise	rest	exercise	rest	exercise
Patients	I	II	I	II	I	II	I	II	I	II
ES	-3	-1	38	41	8	7	98	98	41	41
EJ	-2	-3	22	18	1	0	92	94	32	28
YJ	0	2	34	34	0	3	108	109	42	37
SM	-1	-2	15	9	7	0	83	79	59	54
IL	10	10	69	72	5	4	107	110	13	14
AS	2	-1	24	23	6	3	74	81	47	42
PG	-2	-3	17	16	9	7	57	56	44	41
EK	0	0	25	26	1	5	65	66	46	43
EP	-2	-	11	5	1	3	65	73	41	38
GN	2	2	17	22	1	3	85	86	28	30
Mean	0.4	0.5	27.1	27.1	3.9	3.5	83.4	85.2	39.3	36.8
SD	3.8	4.0	17.0	18.6	3.4	2.4	18.0	17.8	12.5	10.8
Mean diff.										
(I-II) $\pm$ SD	0.2 $\pm$ 1.6	1.4 $\pm$ 4.1	0.0 $\pm$ 3.3	0.8 $\pm$ 3.2	0.4 $\pm$ 3.3	-0.5 $\pm$ 4.5	-1.8 $\pm$ 3.6	-3.2 $\pm$ 3.6	2.5 $\pm$ 2.6	4.4 $\pm$ 3.1
P	NS	NS	NS	NS	NS	NS	NS	< 0.05	< 0.05	< 0.01

Ejection fractions for right and left ventricle in the patients studied

(I = first investigation performed with first pass radionuclide angiography; II = second investigation performed with equilibrium radionuclide angiography; * = not achieved for technical reasons)									
Patients	Work Load W	Right ventricular ejection fraction (%)				Left ventricular ejection fraction (%)			
		At rest		During exercise		At rest		During exercise	
		I	II	I	II	I	II	I	II
ES	15	43	41	35	25	63	57	51	
EJ	15	54	60	51	61	56	60	66	
YJ	20	27	12	25	14	65	-	47	
SM	50	55	60	46	50	74	57	68	
IL	15	10	14	11	16	37	-	49	
AS	25	55	47	-*	47	57	54	57	
PG	40	48	55	48	48	38	43	40	
EK	25	47	56	48	-*	68	53	-*	
EP	40	51	42	49	44	53	57	51	
GN	-	40	54	-	-	-	-	-	
Mean	27	43	44	39	38	55	54	54	
SD	13	14	18	14	17	13	6	10	
Reference values									
Mean		49	43	53	49	56		61	
2 SD		10	10	4	12	16		17	
0		17	12	5	12	12		12	

RIGHT VENTRICULAR EJECTION FRACTION

FIRST PASS

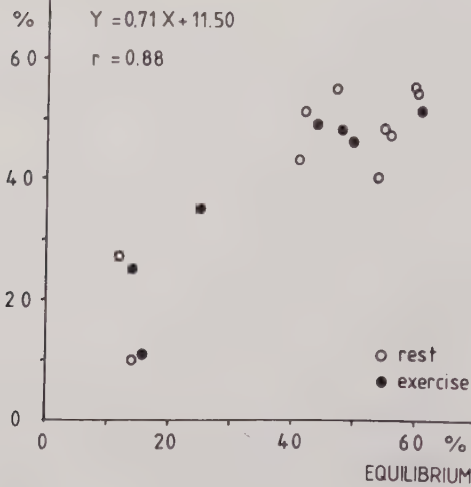


Fig. 1. Correlation between equilibrium and first pass radionuclide right ventricular ejection fraction at rest and during exercise in the patients studied.

Table 4

Coefficients of correlation between RVEF and catheterization variables

CATHETERIZATION VARIABLES	RIGHT	VENTRICULAR	EJECTION	FRACTION
	First	pass	Equilibrium	
	Rest	Exercise	Rest	Exercise
Pressures				
right atrium, mean	- 0.76 *	- 0.84 **	- 0.82 *	- 0.80 *
pulmonary artery, systolic	- 0.88 ***	- 0.85 **	- 0.74 *	- 0.74 *
pulmonary artery, diastolic	- 0.86 **	- 0.76 *	- 0.77 **	- 0.74 *
pulmonary artery, mean	- 0.86 **	- 0.87 **	- 0.75 *	- 0.85 **
Stroke index	0.72 *	0.71 *	0.50 NS	0.33 NS
Pulmonary vascular resistance	- 0.85 **	- 0.82 *	- 0.63 NS	- 0.53 NS
Hematocrit	- 0.58 NS	- 0.81 *	- 0.80 **	- 0.84 **

NS = not significant; * = P < 0.05; ** P < 0.01; *** < 0.001

(C) Relationship between catheterization variables and right ventricular ejection fractions

Statistically significant correlations were found between RVEF, FP and EQ technique, and the simultaneously measured catheterization variables (Table 4). The coefficients of correlation between RVEF, measured with FP technique, and PA mean pressure at rest and during exercise were -0.86 and -0.87 , respectively (Figs. 2 and 3). The corresponding r -values for RVEF, measured with EQ technique, were -0.75 and -0.85 , respectively. The dispersions around the regression lines were, however, considerable.

At rest, one patient had a high RA mean pressure and in this patient RVEF was low. During exercise, five more patients had high RA mean pressures and simultaneously all had a low or decreasing RVEF.

(D) Relationship between pulmonary function, clinical data and right ventricular ejection fraction

There was no significant correlation between RVEF and VC, $FEV_{1.0}$ or heart volume. Nor could any correlation be found between RVEF and arterial tensions of O_2 or CO_2 whether at rest or during exercise. A significant, negative correlation was found between RVEF and the hematocrit value (Table 4). At rest two out of the five patients with a clinical history of right ventricular failure (Table 1) had low RVEF. During exercise, all five had low or decreasing RVEF when measurements were performed with the FP technique. When measured with the EQ technique, four of the five patients with a history of right ventricular failure, had a low or decreasing RVEF during exercise.

(E) Left ventricular ejection fraction

At rest two patients had a low LVEF (Table 3). During exercise a low or a decreased LVEF was found in five out of eight patients. In the two patients with the lowest RVEF, LVEF could not be measured with the FP technique during exercise as the bolus was prolonged too much.

There was no correlation between LVEF and RVEF.

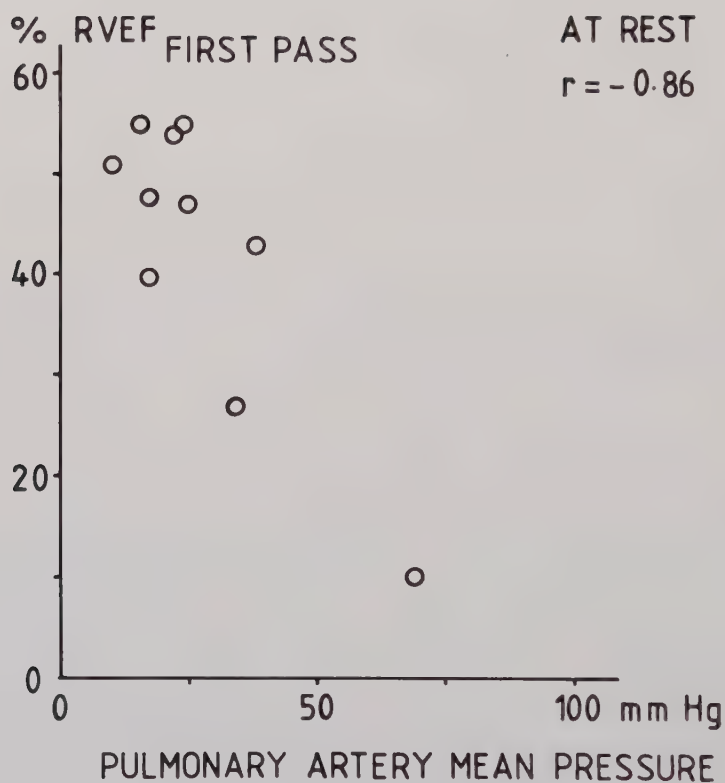


Fig. 2. The correlation between first pass radionuclide right ventricular ejection fraction and pulmonary artery mean pressure at rest.

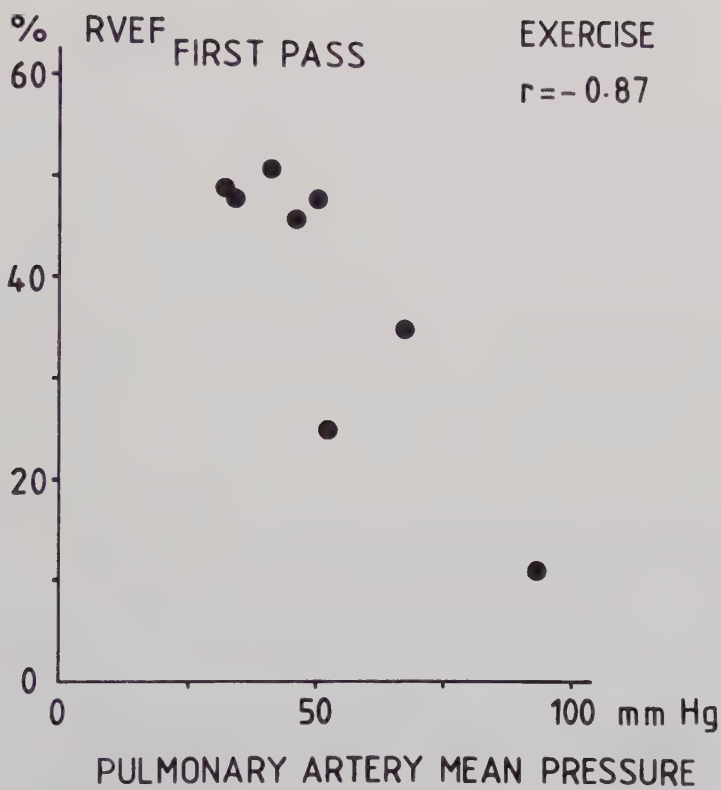


Fig. 3. The correlation between first pass radionuclide right ventricular ejection fraction and pulmonary artery mean pressure during exercise.

DISCUSSION

(A) Catheterization results

The repeated measurements of the catheterization variables showed a good reproducibility. Repeated measurements of catheterization variables at rest and during exercise in patients with lung diseases have been reported by Widimsky, Berglund & Malmberg (1963). They found significantly lower PA pressures and pulmonary vascular resistances during the second exercise measurement and believed that this fall was due to opening or widening of previously closed or constricted lung vessels. The divergent results in the pressure measurements may be due to the higher degree of PH in the present study. Widimsky, Berglund & Malmberg (1963) did not find any difference in heart rate or stroke volume in their patients between the first and the second measurement. The lower stroke volume in the second investigation found in this study, complicates the comparison of the two techniques for measuring RVEF. There was, however, no correlation between the change in stroke index and the change in RVEF in the two investigations. This lack of correlation and the small difference in stroke index ($\leq 10\%$) seemed, however, to justify a comparison of the two techniques to measure RVEF.

(B) Right ventricular ejection fraction (RVEF)

In most previous studies RVEF has been measured with FP radionuclide angiography (Steele et al., 1976; Ellis, Kirch & Steele, 1977; Berger et al., 1978; Berger et al., 1979; Johnson et al., 1979; Slutsky et al., 1980a). The FP technique has the advantage that the right ventricle can be projected with no or minimal overlapping from other cardiac structures containing activity. This is difficult when the EQ technique is used (Dahlström, in press). For repeated studies, the FP technique requires repeated bolus injections of a tracer, which increases the radiation dose to the patient. Furthermore, the background activity in the determinations will differ. In this study these disadvantages have been avoided by using ^{133}Xe at the first measurement (Dahlström, in press). As the circulatory conditions in the first and second measurement were considered equivalent, the FP technique and the EQ technique for assessment of RVEF could be compared. A fair agreement between RVEF measured with the FP and EQ technique was found at rest and during exercise in the present study. At rest, Maddahi et al. (1979) reported a good agreement ($r = 0.95$), when the two

techniques for measuring RVEF were compared in 19 patients with coronary artery disease and one patient with idiopathic pulmonary fibrosis. In the present study the comparison showed a somewhat lower coefficient of correlation ($r = 0.86$) and the dispersion around the regression line was larger. This finding is not surprising, as in patients with PH, right ventricular and right atrial enlargements are often found, thereby causing difficulties in outlining the right ventricle.

Duplicate registrations at rest were used to calculate the standard error of a single determination with the FP and the EQ technique. The absolute value of the standard error of a single determination was found to be 2.6% (Dahlström, in press) and 3.8%, respectively (Dahlström, unpublished data). This difference probably reflects problems in separating the right atrium and the right ventricle and the higher background activity when using the EQ technique. By using a slant-hole collimator the reproducibility for the EQ technique can be improved (Holman et al., 1981).

(C) The relation between catheterization variables and right ventricular ejection fraction

In a previous report by Ellis, Kirch & Steele (1977) in patients with severe chronic airway obstruction, no correlation was found between RVEF and PA systolic or mean pressure at rest. They reported, however, that PA systolic pressure was significantly higher in patients with depressed RVEF than in those with normal RVEF.

The good correlation between RVEF and simultaneously measured PA pressure (Table 4) in the present study cannot be used for prediction of PA pressure from RVEF, since a normal RVEF was found also in patients with PH (Figs. 2 and 3). Thus, RVEF seems to be of less value in detecting or quantifying PH.

At rest, one patient (IL) had a high RA mean pressure and her RVEF was low. During exercise six patients got a high RA mean pressure and all had low or decreasing RVEF. Thus, measurement of RVEF is valuable in revealing right ventricular dysfunction. This dysfunction is seen earlier and more often during exercise. Thus, measurements of RVEF also during exercise may be especially valuable.

(D) The relation between pulmonary function, clinical data and right ventricular ejection fraction

The poor correlation between RVEF and the pulmonary function variables and arterial O_2 and CO_2 tensions confirms the results reported by Slutsky et al. (1980a). The negative correlation between RVEF and hematocrit is interesting but probably only reflects a change in these variables in opposite direction with advancing PH with right ventricular dysfunction.

Berger et al. (1978) reported a low RVEF at rest in all patients with cor pulmonale (history of right ventricular failure and electrocardiographic evidence of right ventricular hypertrophy). In the present study, only one patient (IL) fulfilled their criteria of cor pulmonale. This patient had a low RVEF. Ellis, Kirch & Steele (1977) found a low RVEF at rest in most patients with a history of right ventricular failure. In the present study, two of the five patients with a history of right ventricular failure had a low RVEF at rest, while the other three showed an abnormal RVEF response during exercise, at least when RVEF was measured with the FP technique, again emphasizing the usefulness of measuring RVEF during exercise.

(E) Left ventricular function

Left ventricular function in CPD has been discussed in detail by Widimsky (1981) who emphasized the study by Harris, Segal & Green (1968), reporting the possibility of a falsely high PCV pressure, especially during exercise in patients with CPD. In the present study, all patients had normal PCV mean pressure at rest, while three patients had abnormally high PCV mean pressures during exercise. On the other hand, at rest two patients had low LVEF and during exercise five patients, including those three with high PCV mean pressure, had low or decreasing LVEF. Thus, radionuclide angiocardiology showed left ventricular dysfunction in more patients than did the catheterization technique. The increasing degree of left ventricular dysfunction during exercise in patients with CPD is in agreement with previous reports (Kline et al., 1977; Slutsky et al., 1981). The lack of correlation between RVEF and LVEF is in accordance with the report from Berger et al. (1978).

CONCLUSION

RVEF measured with the FP technique seems to be more reliable due to better reproducibility and somewhat better correlation to hemodynamic variables. By using ^{133}Xe as the tracer, about ten repeated FP studies can be performed before reaching a mean whole body radiation dose similar to that of the EQ study. It is concluded that FP radionuclide angiocardigraphy is the method of choice for measuring RVEF unless LVEF is desired as well, when the EQ technique may be necessary.

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LEFT VENTRICULAR FUNCTION AFTER MYOCARDIAL INFARCTION

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SUMMARY

Left ventricular filling pressure and stroke index were assessed simultaneously with left ventricular ejection fraction in 22 patients who had had their first transmural myocardial infarction about 11 days before the examination. Eleven were classified as anterior myocardial infarctions and 11 as inferior. Left ventricular ejection fraction was determined by equilibrium radionuclide angiography. Significant correlations between left ventricular ejection fraction and left ventricular filling pressure or stroke index were obtained both at rest and during exercise. A more pronounced left ventricular dysfunction was found in patients with anterior myocardial infarction whose left ventricular ejection fraction at rest was $34.9 \pm 3.4\%$ as compared to $52.6 \pm 2.1\%$ in inferior myocardial infarction. The conclusion was that the radionuclide method was as sensitive as the catheterization for detecting left ventricular dysfunction at rest and during exercise in patients with myocardial infarction.

INTRODUCTION

Cohn et al. (1, 2) using ventriculography have convincingly demonstrated the prognostic value of left ventricular ejection fraction in coronary artery disease independent of surgical or medical treatment. In view of the invasive nature of ventriculography there is a need for methods to measure left ventricular ejection fraction less invasively but with similar accuracy. Left ventricular ejection fraction measured with radionuclide methods seems to meet these demands (3, 4).

There is an increasing interest in analyzing the pumping action of the left ventricle during exercise, i.e. dynamic ventriculography (5). Radionuclide methods are well suited for this purpose (6). Determination of left ventricular ejection fraction with the radionuclide method has previously been compared to invasive determinations of pressures and flows, but the measurements have not been performed simultaneously (7, 8).

To our knowledge, this is the first comparison between radionuclide determination of LVEF and invasive determination of pressures and flows performed simultaneously at rest and during exercise in patients with acute myocardial infarction. The influence of the location of the infarctions on left ventricular function was also studied.

MATERIAL AND METHODS

Patients

Twenty-two men with a mean age of 56 years (range 45-67) were examined. They were referred to the Department of Clinical Physiology for hemodynamic evaluation after their first myocardial infarction. All patients were in sinus rhythm and none of them showed any clinical signs of valvular heart disease or lung disease.

The diagnosis of myocardial infarction was established in all patients according to the following three criteria: chest pain, electrocardiographic changes documenting transmural myocardial infarction (i.e. Q-waves and evolutionary ST-T-changes) (9) and typical changes in the serum enzymes aspartase amino-

transferase and lactic dehydrogenase and its isoenzymes. Aspartase aminotransferase was measured at the admission and the following three mornings. Lactic dehydrogenase was measured on the third day. The maximal concentration of the serum enzymes was taken as an index of infarction size (10, 11). Eleven myocardial infarctions were classified as anterior and eleven as inferior (9). Individual data are presented in Table 1. On the 11th day (range 8-19) after the myocardial infarction, left ventricular function was measured simultaneously with the invasive and radionuclide methods both at rest and during exercise.

Catheterization technique

Arterial pressures and blood samples were obtained by a percutaneously inserted brachial artery catheter (PE160). A similar catheter was inserted percutaneously into a cubital vein and passed to the pulmonary artery, controlled with fluoroscopy. The diastolic pressure in the pulmonary artery was taken as left ventricular filling pressure (12, 13). At the end, this pulmonary artery catheter was withdrawn to the right atrium for pressure measurement. The pressures were recorded with conventional equipment (pressure transducer 746 and Mingo-graph 81 from Siemens-Elema AB, Stockholm, Sweden). The supine zero level was taken 5 cm behind the sternum angle. Mean pressures were obtained by electrical damping. Cardiac output was measured by the dye dilution technique (bromsulphalein) (14). Stroke work index (joule/beat/m²) was calculated as (mean brachial artery pressure - left ventricular filling pressure) (mm Hg) x stroke index (ml/m²) x 1.33 x 10⁻⁴.

Radionuclide angiocardiography

Blood pool imaging was performed with in vivo labelled red blood cells with 500 MBq (13.5 mCi) ⁹⁹Tc^m (15). A gammacamera (Radicamera II) with a low energy all purpose parallel-hole collimator was used. The energy window for ⁹⁹Tc^m was set at 140 keV ± 15%. The camera projection during the equilibrium study was a modified left anterior oblique view with a caudal tilt of about 15°. The left anterior oblique angle that optimally separated the ventricles was chosen (about 30°). The dynamic gammacamera data and an R-wave signal from the electrocardiograms were collected in list mode by means of a NUKAB 2530 system. A "hardware zoom" was used. Thus, only counts from the central two-thirds of the 26 cm field of view were collected. In list mode 1.6 million counts (one mag-

TABLE 1
INDIVIDUAL ANTHROPOMETRIC, CLINICAL AND HEMODYNAMIC DATA AT REST AND DURING EXERCISE.

	AGE (YEARS)	LDH (μ KAT/L) (< 8.0)	HEART VOLUME (ML/M ²)	WORKING CAPACITY (W)	LVF		LVP		SI		
					REST (%)	EXERCISE (44-78)	REST (MM HG)	EXERCISE (3-21)	REST (ML/M ²) (28-80)	EXERCISE (43-80)	
NORMAL RANGE											
ANTERIOR MYOCARDIAL INFARCTION											
1 (A)	61	62.0	525	20 E	17	17	16	30	25	30	
2 (B,C)	50	25.3	590	20 R	22	15	14	25	43	33	
3 (B,C,D)	45	45.0	590	20 E	26	28	9	15	20	22	
4	57	19.9	385	20 A	31	25	21	31	37	33	
5	60	19.8	545	40 E	29	26	8	19	45	49	
6	54	11.4	370	40 E	39	50	5	13	46	54	
7	64	19.2	385	40 E	44	47	6	12	32	37	
8 (B)	52	29.0	490	40 R	46	45	10	15	41	45	
9	51	14.2	505	40 E	51	49	5	11	53	55	
10	56	13.8	515	60 W	31	39	13	19	39	43	
11 (E)	62	16.3	420	60 W	48	57	8	6	43	46	
$\bar{X}$	55.6	25.1	481	36	34.9	36.2	10.5	17.8	38.6	40.6	
SE	1.8	4.6	23	5	3.4	4.4	1.5	2.4	2.9	3.2	
INFERIOR MYOCARDIAL INFARCTION											
12 (B,C)	62	25.0	420	20 E	51	57	5	10	39	42	
13	67	13.3	450	20 E	51	55	2	12	47	43	
14	63	15.5	500	20 A	54	38	10	18	38	32	
15	48	21.7	580	40 E	45	43	4	10	48	47	
16	54	10.8	410	40 E	48	69	9	17	59	63	
17	60	26.5	695	40 E	56	49	7	7	48	51	
18	64	20.5	560	40 A	56	53	4	14	53	52	
19	56	10.5	550	40 E	60	52	6	26	48	32	
20	52	15.5	515	60 W	38	41	12	14	50	52	
21	50	38.0	510	60 W	59	75	8	11	42	44	
22 (B,C,F)	52	28.6	590	60 W	61	65	7	8	54	52	
$\bar{X}$	57.1	20.5	526	40	52.6	53.8	6.7	13.4	47.8	46.4	
SE	1.9	2.6	25	5	2.1	3.4	0.9	1.6	1.9	2.8	
SIGNIFICANCE (P)	N.S.	N.S.	N.S.	N.S.	< 0.001	< 0.01	< 0.05	N.S.	< 0.05	N.S.	

LDH = LACTIC DEHYDROGENASE, LVF = LEFT VENTRICULAR EJECTION FRACTION, LVFP = LEFT VENTRICULAR FILLING PRESSURE, SI = STROKE INDEX.

REASONS FOR BREAKING THE EXERCISE TEST: E = EXHAUSTION, R = HEART RATE $> 120/\text{MIN.}$, W = ACHIEVED UPPER WORK LOAD, A = ANGINA PECTORIS, MEDICAL TREATMENT: (A) VERAPAMIL, (B) DIGITALIS, (C) DIURETICS, (D) DISOPYRAMIDE, (E) QUINIDINE, (F) ATENOLOL.

netic disc) were collected giving a collection time of about two minutes with the activity used.

Data reconstruction: As we collected in list mode we afterwards could select the proper R-R-intervals, i.e. the mean $\pm$ about 10%. These R-R-intervals were synchronously added and reconstructed in sequential 40 ms frames (64 x 64 matrix) starting 200 ms before the R-wave. A preliminary region of interest for the left ventricle was chosen. The time activity curve in that region of interest was used to obtain one diastolic and one systolic picture. These were used to define the valve planes, handling them as a movie and subtracting them to give a stroke volume picture. The final end-diastolic region of interest for the left ventricle was then manually outlined from a special diastolic picture. This was built up by squaring the rate of change of counts in x and y directions in the diastolic picture and was used as a help in defining the edges of the left ventricle. The background region of interest was automatically taken two matrix elements wide and two matrix elements outside the left ventricle region of interest not overlapping cardiac structures or great vessels. The time activity curve in the normalized background region of interest, i.e. corrected to the same area as the left ventricle region of interest, did never show any heartsynchronous changes and was subtracted from the left ventricular time activity curve. The left ventricular ejection fraction was then calculated as:

$$\frac{\text{end-diastolic count rate} - \text{end-systolic count rate}}{\text{end-diastolic count rate}}$$

The end-diastolic and end-systolic volume of the left ventricle were calculated from this left ventricular ejection fraction and from stroke volume measured with dye dilution. All volumes were corrected for body surface area.

Radiation dose

The mean whole body radiation dose to the patient due to fluoroscopy is calculated to be about 0.2 mGy (20 mrad) (calculated for one minute fluoroscopy with 75 kV and 0.3 mA - M. Gustavsson: Personal communication). The mean whole body radiation dose due to the radionuclide investigation is calculated to be about 2.3 mGy (230 mrad) (16).

Procedure

The patients were investigated in the catheterization laboratory in the morning. No premedication was given. Prior to the first measurements the patients rested for at least 30 minutes. The equilibrium ejection fraction was always determined simultaneously with the measurements of cardiac output and pressures. The bicycle exercise test was performed in the supine position on the catheterization table with the centre of the pedals elevated 44 cm above the table level. The exercise test started at 20 W and was increased by 20 W every 7 minutes until a maximal level of 60 W was reached. The exercise test was stopped after the maximal work load of 60 W or earlier because of a heart rate exceeding 120/min or because of exhaustion, angina pectoris, arrhythmia or pronounced ST-T-depressions. Physical working capacity was taken as the highest performed work load.

Left ventricular ejection fraction was measured from the 4th to the 6th minute and cardiac output determined during the 5th minute. The pressures were measured immediately before and after the cardiac output and the mean values are given.

Reference values

Reference values for catheterization data were taken from Malmborg (17) with correction for different zero levels. Reference values for radionuclide left ventricular ejection fraction measured with the same technique in 12 normal subjects were $56 \pm 2\%$ at rest and $61 \pm 2\%$ during mild supine exercise (50 W) (Dahlström: To be published).

Statistical methods

Data are expressed as means and standard errors of the mean (SE). Comparisons between groups were made with the aid of Student's t-test and the Wilcoxon rank sum test. Correlation coefficients were obtained using standard regression equations. Probability (P) < 0.05 was considered significant. The average difference in repeated measurements was determined by the arithmetic mean of the absolute numerical difference without regard to sign.

RESULTS

Working capacity

Exercise was stopped in two patients because their heart rate reached 120/min. Two patients stopped due to angina. Five patients reached the upper work load limit of 60 W and 13 stopped because of exhaustion. No one was stopped because of arrhythmia or ST-T-depressions. Individual reasons for stopping exercise are found in Table 1, where the patients are listed according to working capacity.

The relation between results from the catheterization and the radionuclide study

The individual results from the catheterization and radionuclide study are found in Table 1 and figures 1 and 2.

At rest, six patients were found abnormal according to the catheterization results, as four patients had high left ventricular filling pressure and one patient had low stroke index and one had both. Left ventricular ejection fraction was low in all these six patients but also in another two.

During exercise, eight patients were found abnormal according to the catheterization results. All had low stroke index, two of them already at rest, and four patients also had a high left ventricular filling pressure during exercise, three of them already at rest. In these eight patients left ventricular ejection fraction during exercise was low in six patients including all patients with high left ventricular filling pressure but was found normal in two patients with low stroke index. On the other hand, six patients with normal catheterization results had low left ventricular ejection fraction during exercise.

Table 2 shows those correlations between the catheterization variables and left ventricular ejection fraction and left ventricular volumes which were statistically significant.

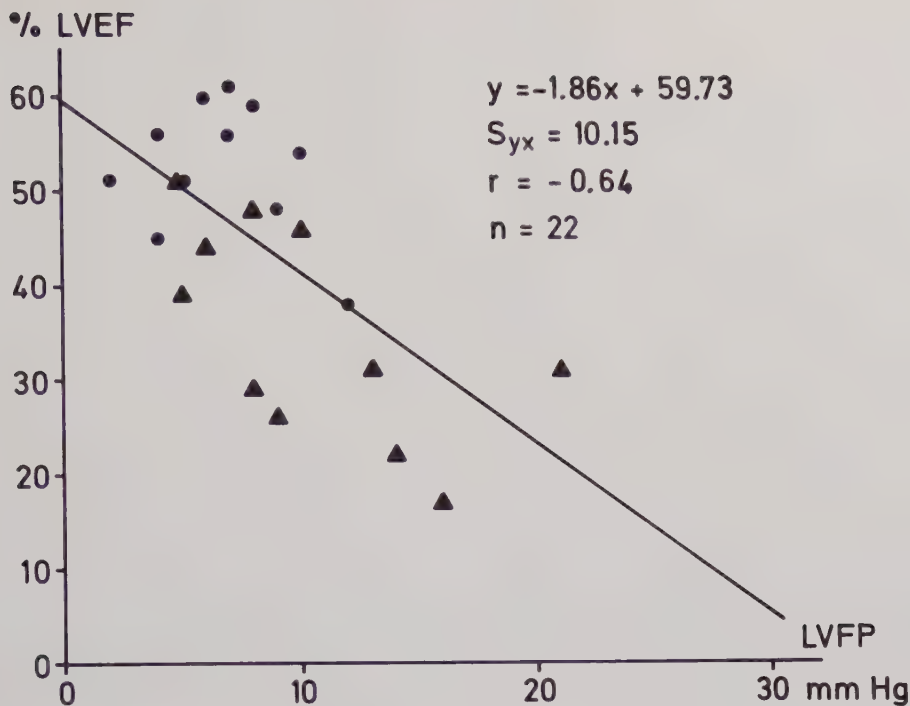


Fig. 1 a. The relation between left ventricular ejection fraction (LVEF) and left ventricular filling pressure (LVFP) at rest. ● = inferior myocardial infarction. ▲ = anterior myocardial infarction.

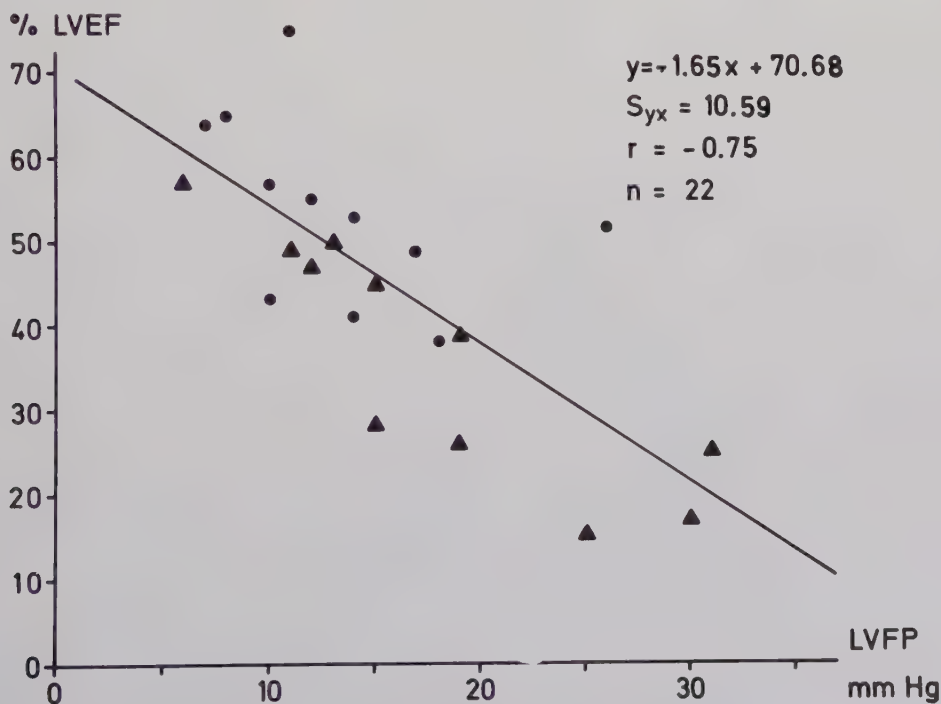


Fig. 1 b. The relation between left ventricular ejection fraction (LVEF) and left ventricular filling pressure (LVFP) during exercise. Symbols as in Fig. 1 a.

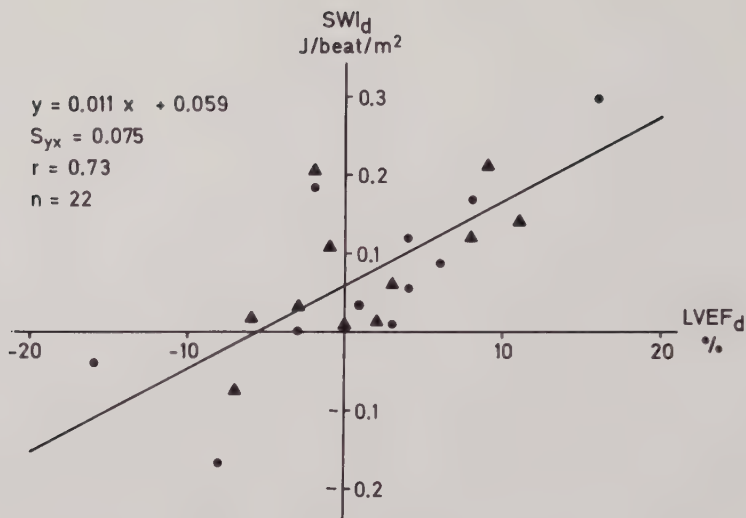


Fig. 2. The relation between the changes in stroke work index (SWI) and left ventricular ejection fraction (LVEF) from rest to exercise. $SWI_d = SWI (\text{exercise}) - SWI (\text{rest})$ and $LVEF_d = LVEF (\text{exercise}) - LVEF (\text{rest})$. Symbols as in Fig. 1 a.

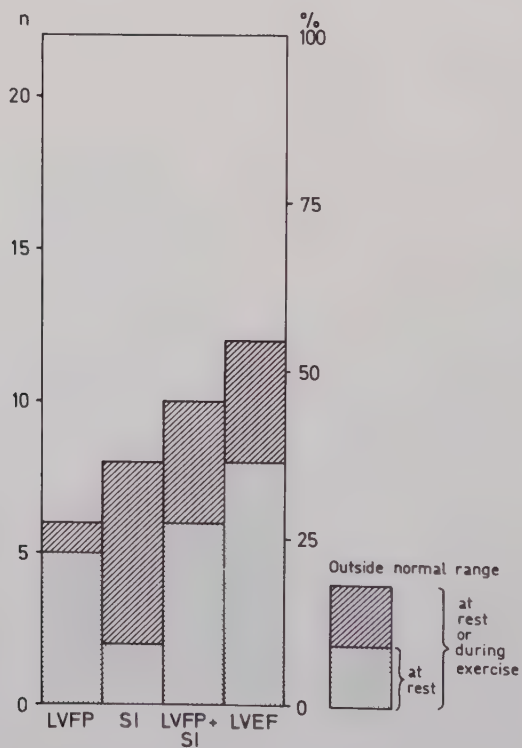


Fig. 3. The number (n) and per cent of patients found to fall outside the normal range at rest and at rest or during exercise at the determinations of left ventricular filling pressure (LVFP), stroke index (SI), LVFP or SI and left ventricular ejection fraction (LVEF).

Table 2

Comparison of various parameters to assess left ventricular function - coefficients of correlations.

	At rest	During exercise	Changes from rest to exercise
	r	r	r
LVEF vs. LVFP	- 0.64	- 0.75	- 0.56
LVEF vs. SI	0.58	0.51	0.62
LVEF vs. SWI	0.43	0.57	0.73
LVEDVI vs. LVFP	0.48	0.57	N.S.
LVESVI vs. LVFP	0.58	0.67	0.48
LVESVI vs. SWI	N.S.	N.S.	- 0.52

LVEF = left ventricular ejection fraction; LVFP = left ventricular filling pressure; SI = stroke index; LVEDVI = left ventricular end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; N.S. = no significant correlation.

The location of the myocardial infarction and its effect upon the hemodynamics

When comparing patients with anterior and inferior myocardial infarctions (Tables 1 and 3) no statistically significant difference was found as regards age, body size or size of the infarction. Neither were there any significant differences in heart volume or working capacity. The catheterization results showed a significantly lower stroke index, higher left ventricular filling pressure and higher heart rate at rest in the anterior myocardial infarction group. These differences decreased during exercise. The mean right atrial pressure which was measured at rest ten minutes after exercise was normal in all patients and did not differ between the groups.

Left ventricular ejection fraction was significantly lower in the anterior myocardial infarction group both at rest ($34.9 \pm 3.4\%$) and during exercise ($36.2 \pm 4.4\%$) compared with the inferior myocardial infarction group, where left ventricular ejection fraction was $52.6 \pm 2.1\%$ and $53.8 \pm 3.4\%$, respectively.

Left ventricular end-systolic volume index was significantly higher in the anterior myocardial infarction group both at rest and during exercise. The end-diastolic volume index tended to be higher at rest and was significantly higher during exercise in anterior infarctions.

DISCUSSION

For comparison of methods to evaluate cardiac function, simultaneous measurements are preferable. When repeated measurements of cardiac function are desired, for example to evaluate changes after interventions, methods which do not affect cardiac function and which have good reproducibility are needed. Left ventricular ejection fraction measured with radionuclide angiocardiology does not interfere with cardiac function and, in our experience, left ventricular ejection fraction assessed with the fixed end-diastolic region of interest method is reproducible. The average difference in repeated measurements was found by us to be 2% at rest and 3% during exercise (Dahlström: To be published). This should be compared to an average difference of 7% when repeated ventriculographies were performed (18). Sorensen et al. (4) also found a good reproducibility with the fixed end-diastolic region of interest method. They showed that this method gave lower values for left ventricular ejection frac-

Table 3

Clinical and hemodynamic data in the anterior
and inferior myocardial infarction groups.

	Anterior myocardial infarction	Inferior myocardial infarction	Significance (P)
Number	11	11	
Body surface area (m ²)	1.94 ± 0.04	1.94 ± 0.06	N.S.
ASAT (μkat/l)	3.74 ± 0.74	3.71 ± 0.55	N.S.
Duration AMI-study (days)	11.1 ± 1.2	10.8 ± 0.5	N.S.
CI (l/min/m ²) at rest	2.83 ± 0.16	2.94 ± 0.09	N.S.
during exercise	4.14 ± 0.30	4.31 ± 0.23	N.S.
Heart rate at rest	75.3 ± 3.7	62.4 ± 1.9	< 0.01
during exercise	103.5 ± 4.2	93.2 ± 3.1	N.S.
RA (mm Hg) at rest	-1.3 ± 0.9	-0.6 ± 0.4	N.S.
APM (mm Hg) at rest	19.1 ± 2.4	14.5 ± 1.1	N.S.
during exercise	32.6 ± 4.1	27.7 ± 2.6	N.S.
ABM (mm Hg) at rest	100.7 ± 3.1	93.1 ± 3.6	N.S.
during exercise	115.6 ± 4.4	113.8 ± 5.7	N.S.
SWI (joule/beat/m ²)			
at rest	0.46 ± 0.04	0.55 ± 0.03	N.S.
during exercise	0.54 ± 0.06	0.62 ± 0.05	N.S.
LVEDVI (ml/m ²) at rest	117.6 ± 11.2	92.8 ± 6.1	N.S.
during exercise	125.9 ± 14.6	89.0 ± 7.2	< 0.05
LVESVI (ml/m ²) at rest	79.0 ± 10.9	44.9 ± 4.9	< 0.01
during exercise	85.3 ± 15.2	42.6 ± 5.7	< 0.05

ASAT = aspartase aminotransferase; AMI = acute myocardial infarction;
CI = cardiac index; RA = mean right atrial pressure; APM = mean pulmonary
artery pressure; ABM = mean brachial artery pressure; SWI = stroke work
index; LVEDVI = left ventricular end-diastolic volume index; LVESVI =
left ventricular end-systolic volume index; N.S. = no significant
difference.

tion compared to ventriculography, even if the correlation between the values is good. Our reference values for left ventricular ejection fraction, $56 \pm 8\%$ (mean $\pm$ SD), are about 15% lower than the values reported for ventriculography, $67 \pm 8\%$ (19). Thus, our values for left ventricular volumes are higher.

The relation between results from the catheterization and the radionuclide study

The correlations between left ventricular ejection fraction and left ventricular filling pressure both at rest and during exercise were significant, even if the dispersion around the regression lines was considerable (Fig. 1 a and b). On the other hand, all patients with a pathologically high left ventricular filling pressure at rest or during exercise had a pathologically low or decreasing left ventricular ejection fraction during exercise. In some patients a pathologically low left ventricular ejection fraction was found, while left ventricular filling pressure was found to be normal.

When comparing stroke index and stroke work index to left ventricular ejection fraction we also found significant correlations (Table 2). A decrease in stroke work index during exercise was always associated with a falling left ventricular ejection fraction (Fig. 2).

All patients with catheterization results indicating left ventricular dysfunction had a pathologically low or decreasing left ventricular ejection fraction except for two patients with low stroke index but normal left ventricular ejection fraction during exercise. The sensitivity of the invasive and radionuclide methods for detecting left ventricular dysfunction is found in Fig. 3. Judging from the catheterization results, 45% of the patients were abnormal, while 55% were abnormal judging from the measurements of left ventricular ejection fraction. There is little reason to suppose that a measurement of left ventricular ejection fraction was too sensitive to detect left ventricular dysfunction, since patients with a clinically ensured myocardial infarction ought to have some disturbance of the left ventricular function. Furthermore, the changes in function measured with the two methods correlated well. Left ventricular volumes did not in any comparison correlate better to the catheterization parameters than did left ventricular ejection fraction (Table 2). The two patients (Nos. 14 and 19) who stopped their exercise because of angina pectoris had the

most pronounced decrease in left ventricular ejection fraction, 16% and 8%, respectively.

We concluded that the non-invasive determination of left ventricular ejection fraction with radionuclide angiocardiology was as sensitive as the standard invasive method in detecting left ventricular dysfunction at rest and during exercise in patients with myocardial infarction.

The location of infarction and its effect upon the hemodynamics

Previous reports have claimed that left ventricular function is more impaired after anterior than inferior infarctions (20, 21). In order to assess the influence of the location of infarction on left ventricular function, the time lap between myocardial infarction and the investigation, the size of the infarction and the condition of the remaining myocardium have to be comparable. In the present study, only patients with their first myocardial infarction and without signs of previous heart disease were compared.

The lower left ventricular ejection fraction and higher left ventricular filling pressure in anterior than inferior myocardial infarctions found by us were in agreement with results published by Hori et al. (22). The incidence of infarctions involving both the right and left ventricle has been reported to be as high as 43% (23). This was most often found in patients with inferior left ventricular infarction (23, 24). The size of inferior left ventricular infarction judged from serum enzymes may thus be overestimated. Infarctions involving the right ventricle, however, usually resulted in a higher right atrial mean pressure (25, 26). We did not find any patient with high right atrial mean pressure so we did not have any evidence of right ventricular infarction in this study, even if it could not be entirely ruled out.

We observed, however, a more impaired left ventricular function in anterior than in inferior myocardial infarctions. This impairment was best seen in the left ventricular ejection fraction.

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LEFT VENTRICULAR FUNCTION AT REST AND DURING EXERCISE IN
CORONARY INSUFFICIENCY - A SIMULTANEOUS EVALUATION BY MEANS
OF RADIONUCLIDE ANGIOCARDIOGRAPHY AND CATHETERIZATION

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SUMMARY

Left ventricular function was assessed simultaneously with heart catheterization and equilibrium radionuclide angiocardiography at rest and during supine exercise in ten patients with effort angina. At rest all had normal hemodynamics. During exercise all developed angina with signs of left ventricular dysfunction in the form of high left ventricular filling pressure, 31 ± 2 mm Hg (mean $\pm$ SEM) and pathological decreases in left ventricular ejection fraction (11 ± 1 per cent units). Left ventricular end-systolic volume increased significantly ($43 \pm 7\%$), but the increase in left ventricular end-diastolic volume ($13 \pm 7\%$) was not significant. The discordance between the changes in left ventricular filling pressure and the changes in left ventricular end-diastolic volume is discussed. Radionuclide angiocardiography revealed left ventricular dysfunction as frequently as did heart catheterization.

INTRODUCTION

The first catheterization study of patients with exercise-induced angina pectoris was published by Müller and Rörvik (1957) who reported an increased pulmonary capillary venous (PCV) mean pressure during angina. Since then extensive hemodynamic studies have been performed in patients with effort angina (Malmborg 1964; McCallister et al. 1968; Wiener, Dwyer, Jr. & Cox 1968; Khaja et al. 1970; Lecerof 1974; Carlens, Hindmarsh & Holmgren 1979). Right heart catheterization is often routinely performed to evaluate cardiac function in patients with coronary artery disease before and after treatment (Friedman 1978).

In recent years radionuclide angiocardiology has been used to assess left ventricular function. Borer et al. (1977) were first to report a decrease in left ventricular ejection fraction (LVEF) during exercise in patients with effort angina in contrast to normal individuals who increased their LVEF.

The purpose of this study was to compare the evaluation of left ventricular function assessed with radionuclide angiocardiology and catheterization technique. Thus, we simultaneously measured left ventricular function with the two techniques at rest and during exercise in patients with coronary insufficiency. To our knowledge, no such comparison with simultaneous measurements has been published previously.

To understand left ventricular performance better it is of great value to obtain knowledge of the left ventricular volumes, particularly the end-diastolic volume. From changes in left ventricular end-diastolic volume and simultaneously determined stroke volume or stroke work, left ventricular function curves, Starling curves, can be derived (Katz 1977). It is, however, difficult to assess left ventricular volumes during exercise. Some measurements have been made using ventriculography (Sharma et al. 1976), echocardiography (Crawford, White & Wray Amon 1979) and radionuclide methods (Rerych et al. 1978; Slutsky et al. 1979).

By combining stroke volume determined with heart catheterization and LVEF assessed with radionuclide angiocardiology it is easy to calculate left ventricular volumes both at rest and during exercise.

MATERIAL AND METHODS

Patients

The patients studied were nine men and one woman with a mean age of 56 years (range 46-71), all with severe effort angina, referred to the Department of Clinical Physiology for evaluation of left ventricular function at rest and during exercise. Their clinical data are given in Table 1. Coronary angiography was performed in seven patients who were candidates for coronary by-pass surgery. Since their effort angina was severe, most patients were treated with various drugs (see Table 1). These drugs were withdrawn at least 12 hours prior to the study. Two patients had bundle branch block at rest. The other eight, including the three patients without coronary angiography, showed transitory ST-depressions during exercise test. All patients were in sinus rhythm and none of them had signs of valvular heart or advanced lung disease.

Methods

Arterial pressures and blood samples were obtained by a percutaneously inserted brachial artery catheter (PE160). A double-lumen Cournand heart catheter was percutaneously inserted into a cubital vein and passed to the pulmonary artery, controlled with fluoroscopy. In the wedge position in the pulmonary artery the PCV mean pressure was measured. The PCV mean pressure and in one patient (No. 1) the diastolic pulmonary artery pressure were taken as an index of left ventricular filling pressure (LVFP) (Jenkins et al. 1970; Falicov & Resnekov 1970). The pressures were recorded with conventional equipment (pressure transducer 746 and Mingograph 81 from Siemens-Elema AB, Stockholm, Sweden). The supine zero level was taken 5 cm behind the sternum angle. Mean pressures were obtained by electrical damping. Cardiac output was measured by the dye dilution technique (bromsulphalein) (Wassén 1956). Cardiac output and heart rate were used to calculate stroke volume in ml which was divided by the body surface area in m^2 to get stroke index (SI). Stroke work index (SWI) (joule /beat/ m^2) was calculated as (mean brachial artery pressure - LVFP) (mm Hg) x SI (ml/ m^2) x 1.33×10^{-4} .

Table 1

Clinical data in the patients studied. M = male; F = female. Medical treatment:
a = digitalis; b = verapamil; c = atenolol; d = propranolol; e = metoprolol;
f = pindolol; g = clofibrat. N.Y.H.A. = New York Heart Association

$\bar{M}$ = mean; SEM = standard error of the mean.

Patient No.	Sex	Age (years)	Body surface area (m ²)	Heart volume (ml/m ²)	Previous myocardial infarction	Medical treatment	Coronary angiography diameter reduction $\geq$ 50%	Functional classification according to N.Y.H.A.
1	M	56	1.98	550	Yes	-	Not performed	III
2	M	46	1.84	500	Yes	b, d	Yes	III
3	M	54	1.59	410	Yes	a, b, g	Yes	III
4	M	58	1.95	470	Yes	b, d, g	Yes	III
5	M	56	2.08	620	Yes	a, c, g	Yes	III
6	M	52	1.93	440	No	e, g	Yes	III
7	M	61	1.95	390	No	-	Yes	II
8	F	51	1.92	410	No	-	Yes	III
9	M	54	2.02	350	No	f, g	Not performed	II
10	M	71	1.74	400	No	a, b, c	Not performed	III
$\bar{M}$		56	1.90	454				
SEM		2	0.05	26				

Relative heart volume in ml/m^2 body surface area was measured in standing position according to Jonsell (1939). The functional capacity limited by angina pectoris was classified according to the New York Heart Association (1955).

Radionuclide angiocardiology

Blood pool imaging was performed with in vivo labelled red blood cells with 500 mBq (13.5 mCi) $^{99}\text{Tc}^{\text{m}}$ (Dahlström et al. 1979). A gammacamera (Radicamera II) with a low energy all purpose parallel-hole collimator was used. The energy window for $^{99}\text{Tc}^{\text{m}}$ was set at $140 \text{ keV} \pm 15\%$.

The camera projection during the equilibrium study was a modified left anterior oblique (LAO) view with a caudal tilt of about 15° . The LAO-angle which optimally separated the ventricles was chosen (about LAO 30°). The dynamic gamma-camera data and an R-wave marker from the simultaneously recorded ECG were collected in list mode by means of a NUKAB 2530-system. A "hardware zoom" was used. Thus, only data from the central two-thirds of the 26 cm field of view were collected. In list mode 1.6 million counts (one magnetic disc) were collected giving a collection time of about 2 minutes for each measurement of the ejection fraction.

Data reconstruction

As we collected in list mode we afterwards could select the proper R-R-intervals, i.e. the mean R-R-interval $\pm 10\%$. These R-R-intervals were synchronously added and reconstructed in sequential 40 msec frames (64×64 matrix) starting 200 msec before the R-wave. A preliminary region of interest (ROI) for the left ventricle was chosen. The time activity curve in that ROI was used to obtain one diastolic and one systolic picture. These were used to define the valve planes better, handling them as a movie and subtracting them to give a stroke volume picture. The final fixed end-diastolic ROI for the left ventricle was then manually outlined from a special diastolic picture. This was built up by squaring the rate of change of counts in x and y direction in the diastolic picture and was used as an aid in defining the edges of the left ventricle. The background ROI was automatically taken two matrix elements wide and two matrix elements outside the left ventricle ROI not overlapping cardiac structures or great vessels. The time activity curve in the background ROI, normalized to the

same area as the left ventricle ROI, did not show any heart synchronous changes and was subtracted from the left ventricle time activity curve.

The LVEF in per cent was then calculated as:

$$\frac{\text{end-diastolic count rate} - \text{end-systolic count rate}}{\text{end-diastolic count rate}} \times 100$$

The end-diastolic (LVEDVI) and end-systolic volume (LVESVI) of the left ventricle were calculated from this LVEF and stroke volume measured with dye dilution. All volumes were corrected for body surface area.

Radiation dose

The mean whole body radiation dose to the patient due to fluoroscopy for the catheterization is estimated to be about 20 mrad = 0.2 mGy (calculated for one minute fluoroscopy with 75 keV and 0.3 mA - Monica Gustavsson, personal communications). The mean whole body radiation dose for the radionuclide investigation is calculated to be about 230 mrad = 2.3 mGy (Johansson, Mattsson & Nosslin 1981).

Procedure

The studies took place in the morning. No premedication was given. After the catheters had been inserted the patients rested for 30 min. prior to the control measurements. Then exercise for three to eight min. followed and finally the recovery measurements were performed at rest ten min. after exercise.

LVEF was always determined simultaneously with the cardiac output and the pressures. The bicycle exercise test was performed in supine position on the catheterization table with the centre of the pedals elevated 44 cm above the table level. The exercise test was performed at a previously tested level which the patients could sustain for at least three min. The data for each LVEF determination were collected during about two min. Cardiac output was determined in the middle of these two min. The PCV mean pressure was followed continuously and the other pressures were measured immediately before and after the measurements of cardiac output and the mean values are given.

Reference values

Reference values for catheterization data were taken from Malmberg (1964) with correction for different zero levels. Reference values for radionuclide LVEF measured with the same technique in 12 healthy subjects were $56 \pm 2\%$ at rest and $61 \pm 2\%$ during mild supine exercise (50 W) (Dahlström et al. To be published). The standard error of a single determination calculated from duplicate measurements is 2.0 ml/m^2 for SI and for LVEF at rest and during exercise 1.8% and 3.0%, respectively (Dahlström et al. To be published).

Statistical methods

Data are expressed as means and standard errors of the mean (SEM). Changes in individual patients were tested by the paired t-test. Probability (P) < 0.05 was considered significant. The standard error of a single determination (e) assessed from duplicate measurements was calculated according to Dahlberg (1948) using the formula:

$$e = \sqrt{\frac{\sum d^2}{2n}}$$

where n is the number of duplicate measurements and $\sum d^2$ is the sum of the squares of the differences.

RESULTS

In Fig. 1 the values for LVEF and LVFP at rest, during and after exercise can be followed for one patient (No. 3). The appearance, the maximum and the disappearance of the angina and the corresponding electrocardiographic changes are also shown.

At rest all patients had normal LVFP, SI and LVEF, see Table 2, where individual results are given. During supine exercise (mean working level 30 W) all patients developed angina. LVFP increased to a pathologically high level in all patients, from $6 \pm 1 \text{ mm Hg}$ to $31 \pm 2 \text{ mm Hg}$, $P < 0.001$. SI fell in all except one patient and the mean value changed from $50 \pm 3 \text{ ml/m}^2$ to $44 \pm 3 \text{ ml/m}^2$, $P < 0.01$ (Fig. 2). SWI decreased during exercise in all patients whose SI fell, the mean decrease being 14%, $P < 0.05$ (Fig. 3). LVEF decreased significantly in all patients by a mean of 11 % units, $P < 0.001$ (range 6-18) (Fig. 2). There

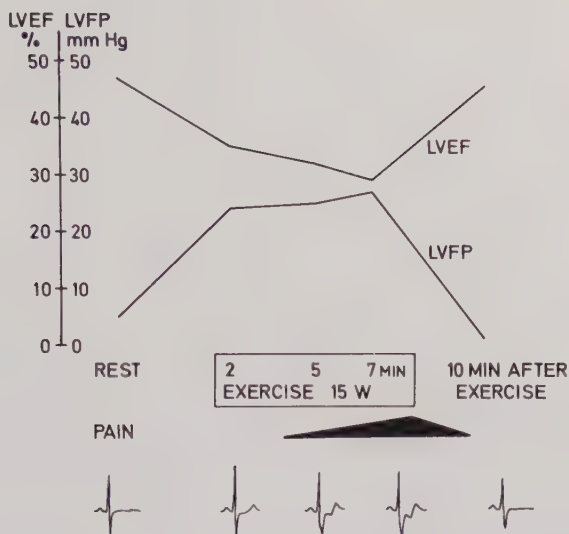


Fig. 1. Repeated registrations of left ventricular ejection fraction (LVEF), left ventricular filling pressure (LVFP), pain and ECG at rest, during exercise and after exercise in one patient (No. 3).

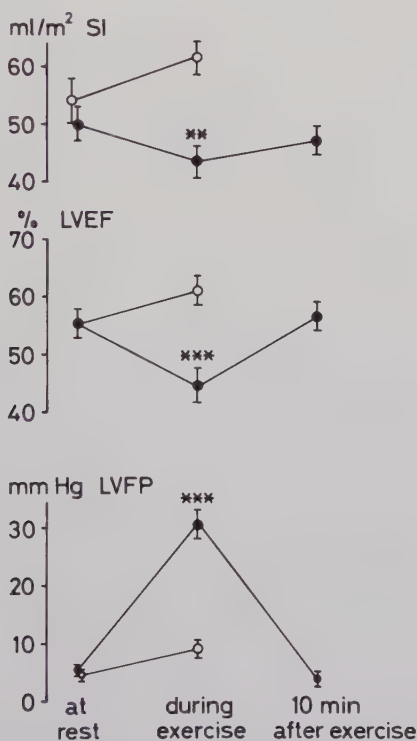


Fig. 2. Mean $\pm$ standard error of the mean for stroke index (SI), left ventricular ejection fraction (LVEF) and left ventricular filling pressure (LVFP) at rest, during exercise and after exercise in normal individuals (o) and in patients with effort angina (●). In the patient group, significant changes from rest are shown as: ** = $P < 0.01$ and *** = $P < 0.001$. Reference values were obtained from Malmberg (1964).

Table 2

Hemodynamic data in the patients studied at rest and during exercise with effort angina. LVEF = left ventricular ejection fraction. PCV = pulmonary capillary venous mean pressure.

$\bar{M}$ = mean; SEM = standard error of the mean.

Patient No.	Exercise level (W)	LVEF (%)		PCV (mm Hg)		Stroke index (mL/m ²)		Heart rate (min ⁻¹)		Mean brachial artery pressure (mm Hg)	
		rest	exercise	rest	exercise	rest	exercise	rest	exercise	rest	exercise
1	40	60	52	6	26	48	32	62	105	85	105
2	50	45	39	3	26	54	46	53	95	92	116
3	15	47	29	5	27	53	43	61	111	95	134
4	10	70	58	9	46	49	37	67	90	134	178
5	20	59	50	5	21	38	36	68	75	100	116
6	30	52	37	7	28	70	68	66	90	108	131
7	50	48	36	6	30	52	46	82	106	118	136
8	10	65	57	6	30	50	43	66	94	115	139
9	50	50	43	3	40	52	50	65	99	119	115
10	25	59	44	5	31	34	37	62	76	102	132
$\bar{M}$	30	56	45	6	31	50	44	65	94	107	130
SEM	5	3	3	1	2	3	3	2	4	5	6

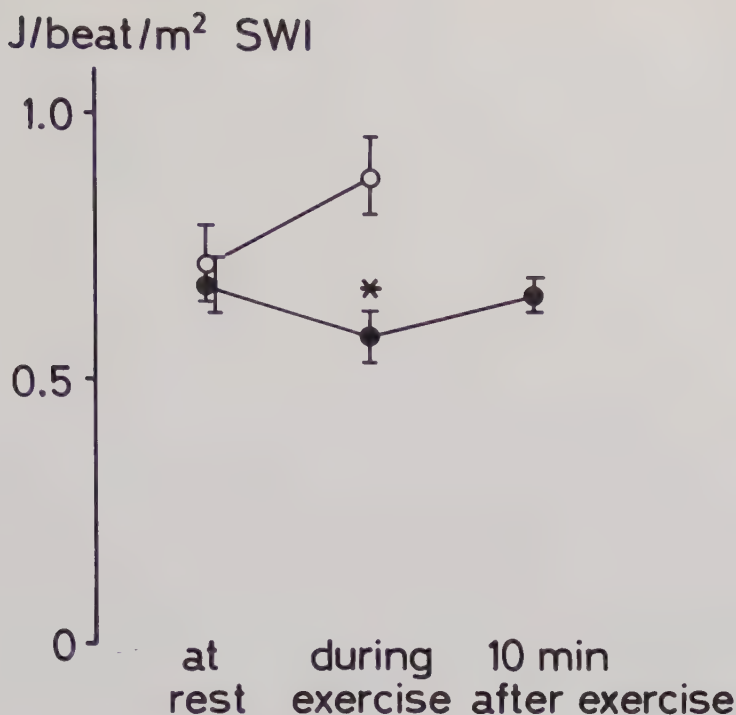


Fig. 3. Mean $\pm$ standard error of the mean for stroke work index (SWI) at rest, during exercise and after exercise in normal individuals (o) and in patients with effort angina (●). In the patient group, significant changes from rest are shown as: * = $P < 0.05$. Reference values were obtained from Malmberg (1964).

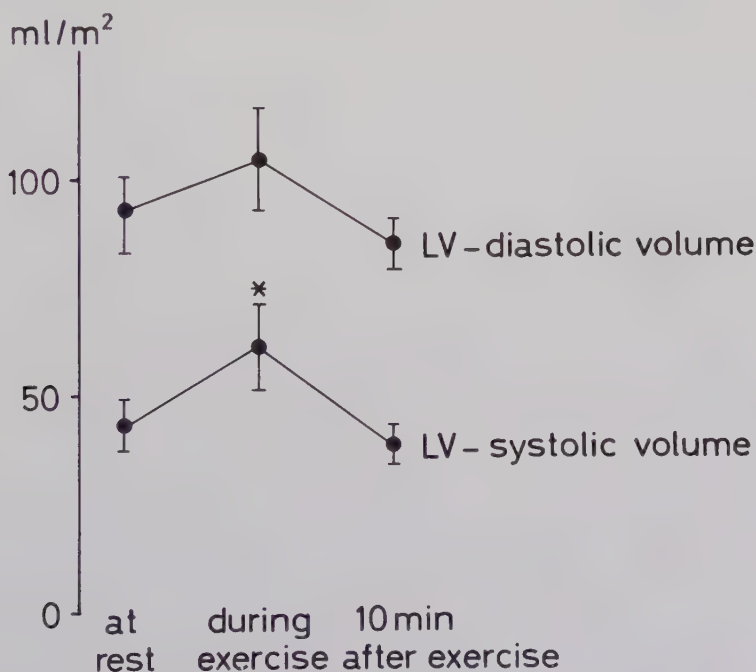


Fig. 4. Mean $\pm$ standard error of the mean for left ventricular (LV) end-diastolic volume index and left ventricular end-systolic volume index at rest, during exercise and after exercise in patients with effort angina. * $P < 0.05$ denotes significant change from rest.

was a significant increase in LVESVI during exercise ($+ 43 \pm 7\%$), $P < 0.05$ while the change in LVEDVI was not significant ($+ 13 \pm 7\%$) (Fig. 4). Ten min. after exercise when all patients were relieved from angina, LVFP, SI, SWI, LVEF and the left ventricular volumes had returned to resting levels (Figs. 2, 3 and 4). There was no significant correlation ($r = 0.10$) between the changes in LVEF and the changes in LVFP during exercise.

DISCUSSION

From several studies it is well-known that patients with effort angina often have normal left ventricular function at rest (Müller & Rörvik 1957; Malmborg 1964; McCallister et al. 1968; Wiener, Dwyer, Jr. & Cox 1968; Khaja et al. 1970; Lecerof 1974; Carlens, Hindmarsh & Holmgren 1979).

During exercise, however, when angina pectoris appears, most patients show hemodynamic signs of left ventricular dysfunction. This dysfunction is usually seen as an increased PCV mean pressure (Friesinger 1977).

Several studies have reported that LVEF decreases during exercise in patients with effort angina (Borer et al. 1977; Rerych et al. 1978; Slutsky et al. 1979). These patients often will have normal LVEF at rest. Comparison between LVEF and catheterization results at rest and during exercise has been given by Sauer et al. (1978). Their measurements were, however, not obtained at the same time, so simultaneous measurements of LVFP, SI and LVEF in effort angina have not been reported until now.

In the present study radionuclide angiocardiology and invasive measurements were performed simultaneously. At rest we found normal LVEF and normal hemodynamics in all patients including the five patients with previous myocardial infarction. Normal hemodynamics at rest in spite of previous myocardial infarction are a common finding when the acute stage has passed (Malmcrona 1964).

During exercise all patients in this study developed angina and everyone showed hemodynamic signs of left ventricular dysfunction with pathologically high LVFP. SI and SWI also fell in all except one patient. LVEF decreased in all patients. Ten min. after exercise when angina had disappeared both catheterization and radionuclide data had returned to resting levels. Thus, radio-

nuclide LVEF demonstrated left ventricular dysfunction during exercise as frequently as data obtained by catheterization.

The lack of correlation between the changes in LVEF and the changes in LVFP during exercise indicates that LVEF and LVFP reflect different aspects of left ventricular function. LVEF describes the systolic function of the left ventricle and left ventricular end-diastolic pressure, in this study estimated from PCV mean pressure or pulmonary artery diastolic pressure, is an indicator of the diastolic properties of the left ventricle.

LVEF determined with the fixed end-diastolic ROI-method, used by us, is very reproducible (Dahlström et al. To be published). LVEF obtained by this method has been shown to correlate well with contrast angiography (Sorensen et al. 1979), even if the absolute value for LVEF usually is somewhat lower with the radionuclide method. Our reference values for LVEF are about 15% lower compared to reference values given for contrast angiography (Yang et al. 1972) and thus the left ventricular volumes calculated from LVEF and SI are higher.

The decreased LVEF during exercise in this study was caused mainly by an increase in LVESVI (Fig. 4). The LVEDVI also tended to increase but the results were not conclusive. Sharma et al. (1976) using contrast angiography showed that in normal individuals LVEDVI and LVESVI decreased immediately after exercise. In patients with ischemic heart disease and effort angina the left ventricular volumes increased. Their volumes were, however, not determined during exercise but immediately after. Determinations performed after exercise may not give the same results as those performed during exercise. Rerych et al. (1978) used the first pass radionuclide technique in anterior projection to assess LVEDVI using a length-area method. They investigated normal individuals and patients with coronary insufficiency at rest and during sitting exercise. They found increased LVEDVI, LVESVI and SI in patients during exercise with angina. In normal individuals LVESVI decreased and LVEDVI and SI increased. Their study is, however, not quite comparable to ours since heart volume differs in upright and supine position (Holmgren & Ovenfors 1960) and the changes in SI from rest to exercise are more pronounced in upright position (Bevegård et al. 1960). Slutsky et al. (1979) used a count-based method for comparing left ventricular volumes at rest and during exercise in supine position. They found an increase in end-systolic volume during exercise but no significant change in end-dias-

tolic volume in patients with coronary artery disease and angina during exercise. Their results are thus in agreement with ours.

Left ventricular function curves - Starling curves - are often used to describe left ventricular function. Usually SI or SWI, on the ordinate, is plotted against end-diastolic fiber length, i.e. LVEDVI. As LVEDVI is difficult to measure, left ventricular end-diastolic or PCV mean pressure is used as an index of LVEDVI (Katz 1977). In these patients with effort angina, LVFP and LVEDVI did not change parallelly. In all patients LVFP increased pathologically. However, in four patients (Nos. 1, 2, 4 and 8, Fig. 5) LVEDVI fell slightly during exercise. In these four patients the increased LVFP implies a lower diastolic left ventricular compliance during angina. Lower ventricular compliance during angina, induced by atrial pacing, has been reported previously (Barry et al. 1974).

A decrease in SWI with little change in LVEDVI, a measure of preload, was found during exercise in some patients (Nos. 2, 4, 5, 8 and 9 in Fig. 5). If afterload did not increase in these patients, the decrease in SWI would mean a change to a lower Starling curve, i.e. a decrease in contractility (Katz 1977). Afterload, here measured as brachial artery pressure, did not increase in patient No. 9. Thus, contractility decreased in this patient. As brachial artery pressure increased in the other patients, the conclusions regarding decreased contractility must be drawn with caution. The fact that SI was used in the calculations of both SWI and LVEDVI, should also be considered in the evaluation of a change in contractility from Fig. 5. Anyhow no signs indicating increased contractility during exercise, usually found in healthy individuals, could be found in the patients studied.

Except for a more pronounced decrease in SI during exercise we could not find any significant difference in clinical or hemodynamic characteristics between the patients who fell in LVEDVI during exercise compared to those who increased LVEDVI. The clinical implication of these results is thus not known now. A follow-up of the clinical course is necessary to evaluate these findings properly.

LVEF determined with radionuclide methods is easily performed both at rest and during exercise. This study and our previous study in patients with myocardial infarction (Dahlström et al. To be published) show that measurements of LVEF

with the radionuclide method will detect left ventricular dysfunction as often as cardiac catheterization. Thus, this radionuclide method, painless and physiological, should be suitable for assessment of left ventricular function at rest and during exercise in the investigation of coronary artery disease. As the radiation dose is low and the investigation easy to repeat the effect of treatment can be followed.

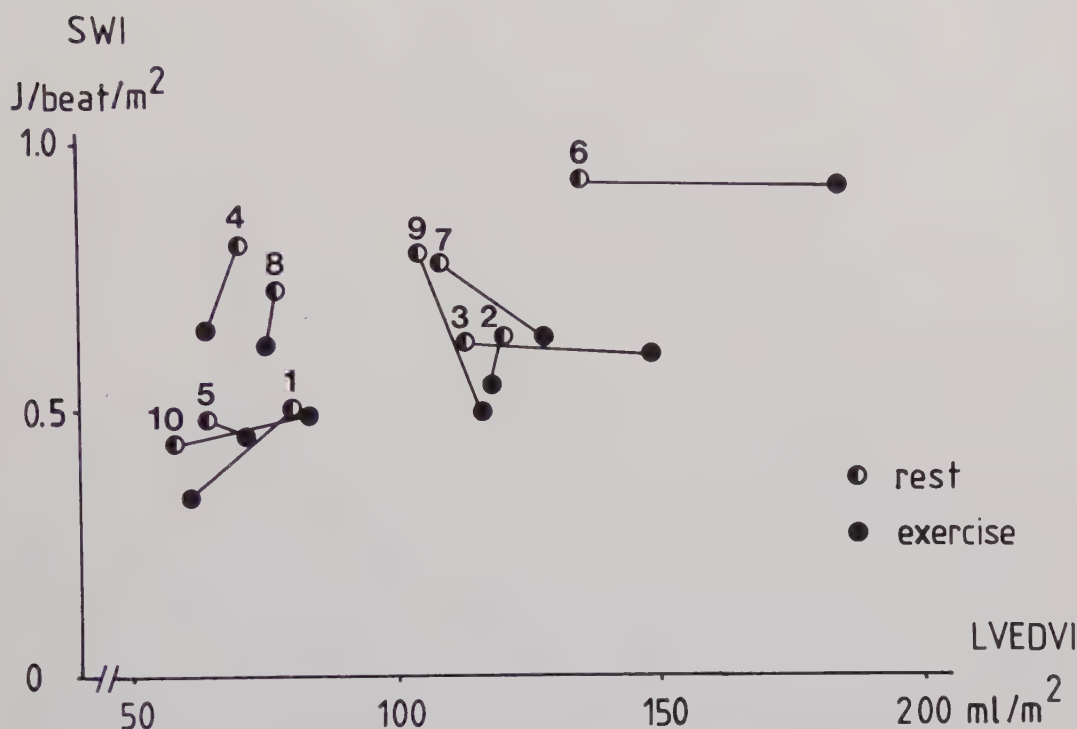


Fig. 5. The changes from rest to exercise in left ventricular stroke work index (SWI) (joule/beats/m²), and left ventricular end-diastolic volume index (LVEDVI) (ml/m²). The patients are identified by the same figures as in Tables 1 and 2.

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